Proceedings of a Conference

Known Effects of Low-Level Radiation Exposure

Health Implications of the TMI Accident

April 1979

U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE

Public Health Service

National Institutes of Health

These proceedings were prepared as a result of a conference held in April 1979 by the Mideast Center for Radiological Physics, Allegheny General Hospital, Pittsburgh. The seminar provided comprehensive information to physicians and public health officials on known effects of low-level radiation. The Mideast Center for Radiological Physics is a contractor (NO1-CN-45148) of the Division of Cancer Control and Rehabilitation, National Cancer Institute.

Proceedings of a Conference

Known Effects of Low-Level Radiation Exposure

Health Implications of the TMI Accident

April 1979

Preventive Medicine Branch

Division of Cancer Control and Rehabilitation

National Cancer Institute

Bethesda, Maryland

P. K. Shrivastava, Ph.D., Editor, MidEast Center for Radiological Physics

Winfred F. Malone, Ph.D., M.P.H., NCI Project Officer

U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE

Public Health Service

National Institutes of Health

NIH Publication No. 80-2087

January 1980

PREFACE

I am pleased to make available these Proceedings on the known effects of low level radiation. This conference was held in Pittsburgh, Pennsylvania, on April 25, 1979, to inform local physicians and public health officials on the known effects of low level radiation exposures.

At the dose rates compatible with maximum permissible exposure levels for radiation workers (5 rems per year to the whole body), the risks of radiation injury are generally assumed to be limited to those types of effects that may result from alterations in individual cells, damaged singly or in small numbers. Included in this category are carcinogenic, teratogenic, and heritable (mutagenic) effects, the frequency of which is generally assumed for purposes of public health policy to increase as a function of dose, without a threshold.

Quantitative estimates of the risks of the carcinogenic effects of low-level radiation have been based largely on linear nonthreshold extrapolations from observations of effects in irradiated human populations exposed for the most part at relatively high doses and dose rates. Based on these extrapolations, the overall lifetime risk of fatal cancer in a population of all ages has been estimated to approximate 200 ($\pm$100) cases per million persons per rem to the whole body. According to this estimate, roughly 1-2 percent of naturally occurring cancers are theoretically attributable to natural background radiation, the exposure to which averages about 100 millirems per year. While the above estimates are applicable to the total population, the risk appears to vary appreciably with age at the time of irradiation and with the anatomical distribution of the dose, not all organs being equally susceptible to radiation carcinogenesis.

Estimates of the risks of heritable effects depend primarily on extrapolation from observations in experimental animals, reinforced by studies of radiation-induced cytogenetic changes in human cells. Based on these sources of evidence, it has been estimated that some form of genetic detriment would affect roughly one in every 10,000 liveborn children in the first generation per rem of parental radiation, with the risk increasing to values several times larger on irradiation of successive generations to genetic equilibrium. According to this estimate, less than 5 percent of naturally occurring genetic diseases are theoretically attributable to natural background radiation.

Numerical estimates of the risks of teratogenic effects of low-level radiation are not available in a form comparable to the above risk estimates for carcinogenic and mutagenic effects. From available evidence, however, it has been tentatively inferred that the risks of teratogenic

effects under conditions of low-level irradiation are of the same order of magnitude per unit dose, or smaller, than those of carcinogenic or mutagenic effects.

Arthur C. Upton, M.D.
Director
National Cancer Institute

AUTHORS

ABRAHAMSON, SEYMOUR, PH.D.
Professor of Zoology & Genetics
University of Wisconsin
Madison, Wisconsin

BOND, VICTOR, M.D.
Associate Director
Brookhaven National Laboratory
Upton, Long Island, New York

BRENT, ROBERT, M.D.
Chairman, Dept. of Pediatrics
Thomas Jefferson University
Philadelphia, Pennsylvania

FABRIKANT, JACOB I., M.D., PH.D.
Professor of Radiology
Donner Laboratory and School of Medicine
University of California, Berkeley, CA
University of California, San Francisco, CA

KROHMER, JACK, PH.D.
Professor of Radiology
Chairman, Division of Radiologic Physics
Wayne State University
Detroit, Michigan

SHRIVASTAVA, PRAKASH, PH.D.
Director, Mideast Center for Radiological Physics
Allegheny General Hospital
Pittsburgh, Pennsylvania

WALD, NIEL, M.D.
Professor & Chairman
Department of Radiation Health
University of Pittsburgh
Pittsburgh, Pennsylvania

INTRODUCTION

The residents of Pennsylvania have survived the immediate impact of the Three Mile Island (TMI) accident, but they have been left confused by the controversy regarding its impact on their future health. For years to come, physicians will be asked if some specific sickness is not due to their exposure. The seminar on "Known Effects of Low Level Radiation Exposure" held in Pittsburgh, PA on April 25, 1979 and preparation of these proceedings was undertaken by the Mideast Center for Radiological Physics to prepare the health professionals for these questions.

Our objective has been to provide physicians, health professionals and concerned citizens with accurate up-to-date information in simple terms. It is hoped that information provided will benefit them to more knowledgeably handle inquiries from their patients.

The Mideast Center for Radiological Physics undertook this project because it is one of six regional centers established in 1974 by the Division of Cancer Control and Rehabilitation of the National Cancer Institute. One of its charges is to act as a resource for education and consultation to the medical community in matters related to radiation and health.

To accomplish our objective, we invited very distinguished and knowledgeable experts in the field. Each chapter of these proceedings is based on the presentations by these experts and includes the questions and answers from the audience.

I sincerely hope that this material will aid in better informing the public and help allay any unnecessary fears resulting from the TMI accident without, of course, minimizing any real ones.

A large number of persons helped me in arranging the meeting. I wish to express my gratitude to Dr. Diane Fink, Director of DCCR and Dr. Arthur C. Upton, Director of NCI, for their support and encouragement. Advice from Mr. Lad Grapski, Drs. J. P. Concannon, L. M. Schiffer, C. R. Joyner, S. W. Lesher, Allegheny General Hospital, Dr. L. M. Bates, AAPM CRP Coordination Program and Dr. W. F. Malone, DCCR, NCI, was invaluable in organizing the seminar. I received vital, unflinching support from Mr. John Sacuto and his staff from the Community Relations Office at Allegheny General Hospital. I am very grateful to the authors for accepting the invitation at such short notice and to Dr. Gordon MacLeod, Secretary of Health, Commonwealth of PA, for agreeing to be the luncheon speaker. I am specially thankful to Mrs. Anne Zinsser for her patience and able assistance in preparing these proceedings.

Prakash N. Shrivastava, Ph.D.

CONTENTS

KNOWN EFFECTS OF LOW LEVEL RADIATION EXPOSURE; HEALTH IMPLICATIONS OF TMI ACCIDENT

Effects of Low Level Radiation - Introductory Overview

Prakash N. Shrivastava, Ph.D.

Radiation energy when absorbed in living tissues is known to produce (1) acute somatic effects, (2) late somatic effects, (3) developmental effects and (4) genetic effects.

These effects depend upon the quantity of radiation (i.e., dose or exposure) and the quality of radiation (i.e., the type of particle or photon, and its energy spectrum).

Different quality beams may produce different amounts of biological effect even if the same amount of energy is absorbed. In biology, this dependence on beam quality is quantitatively expressed by a number called Relative Biological Effectiveness 'RBE'. In human health applications, the beam effectiveness is referred to as the Quality Factor 'QF'. A 200 KVP x-ray beam is conventionally used as a standard (QF=1). The QF for other beams is expressed relative to this standard.

A quantity called Dose Equivalent summarizes the net effect of the dose and Quality Factor. Thus, the Dose Equivalent constitutes an estimate of the radiation hazard. The unit of Dose Equivalent is the 'rem' (radiation equivalent man). The radiation hazard to a large population is often expressed in "person rems". In such discussions, one assumes an equal social impact for 1 rem to 2,000 persons vs. 2 rems to 1,000 persons (2,000 person rems).

Exposure in Dose Equivalent (rem) = Dose in rads x QF

A 'rad' is the unit for absorbed dose. One 'rad' is equal to 100 ergs absorbed energy per gram of tissue.

If some amount of radiation traverses air rather than tissue, it ionizes the air. The extent of ionization produced is used to measure the amount of radiation and is called "Exposure", which is expressed in units of Roentgens (R).

The amount of energy absorbed in tissue exposed to 1 Roentgen depends upon the type of tissue and also the quality of radiation. For χ and γ rays in soft tissue, 1 R exposure results in somewhere between .9 - .98 rads of absorbed dose. Thus, using Roentgens rather than rads to specify dose is often close but never exact.

A. Our knowledge of radiation dose and its effect may be considered in three groups:

I. High dose effects (exposure above 25 rems)
II. Intermediate dose effects (5-25 rem exposures)
III. Low dose effects (exposure below 5 rems)

I & II. HIGH AND INTERMEDIATE DOSE EFFECTS

A great deal of knowledge and experience is available for effects on human tissues at exposures above about 5 rems. (See Table 1) The sources of such data include:

1. Survivors of the atomic bombing in Hiroshima and Nagasaki.

2. Children exposed prenatally as a result of abdominal x-ray examination of the mother during pregnancy.

3. Children treated for enlarged thymus glands by irradiation of their thymus.

4. Adults who receive x-ray treatment of the spine for ankylosing spondylitis.

5. Adults subjected to multiple fluoroscopies in pneumothorax treatment of tuberculosis.

6. Women treated with x-rays for post partum mastitis.

7. Adults receiving radioactive iodine for treatment of thyroid conditions.

8. Individuals with body burdens of radium.

9. Uranium miners exposed to high levels of radiation gasses and particles.

In addition to such human data based on exposures under non-experimental conditions, there exist observations and vast quantitative data on animals exposed to radiation under controlled laboratory conditions. The results may be summarized as follows:

1. Acute somatic effects (i.e., radiation sickness like nausea, vomiting, dehydration, anemia, hemorrhage, etc.) occur at single whole body doses, above 50 or 100 rems.

2. Late somatic effects (i.e., induction of cancer, leukemia, cancers of the thyroid, breast or lung) involve doses of 50 rems or more delivered at a high rate in a short period of time.

3. Developmental effects (skeletal, nervous system, and other malformations) are known to occur in humans from prenatal irradiation in the womb or in young children for doses over 50 rems. Experiments suggest that doses as low as 5 rems in animals can result in such effects.

Table 1

Findings of Epidemiological Studies of Cancer in Irradiated Populations

Subject of study	Follow-up time (yr)	Dose (R or rads)	No. of persons[a]	Form of cancer	No. of cases: Observed in exposed group[b]	No. of cases: Expected if not exposed[c]
1. Hiroshima and Nagasaki A-bomb survivors (bomb exploded 1945). Brill et al., 1962	5-13	0-20	85,070	Leukemia	21	19.1
		21-80	13,184	Leukemia	6	3.0
		81-320	8,695	Leukemia	24	2.0
2. Hiroshima and Nagasaki A-bomb survivors (women). Wanebo et al., 1968	13-21	0-9	3,082	Breast cancer	3	7.3
		10-39	1,262	Breast cancer	5	3
		40-89	857	Breast cancer	2	2
		90-199	802	Breast cancer	5	2
		>200	841	Breast cancer	6	2.3
		Unknown	840	Breast cancer	2	2.3
		Unexposed control	2,458	Breast cancer	2	6.1
3. Hiroshima and Nagasaki A-bomb survivors exposed prenatally. Jablon and Kato, 1970	10	>64,500 person-rads[d]	1,292	All cancers	1	0.75
4. Japanese A-bomb survivors exposed within 1400 m of detonation (died 1950-1962). Angevine and Jablon, 1964	17		1,215 autopsies	All cancers, except leukemia	61	56.8
5. Children exposed prenatally due to abdominal x-ray to mother (exposed 1945-1956 and died before end of 1958). Court Brown et al., 1960	2-12		39,166	Leukemia	9	10.5
6. Children exposed prenatally (born in 1947-1954 and died before end of 1960). MacMahon, 1962	4-13	1-2	77,000[e]	All cancers	85	60
7. Infants who received irradiation of chest before age 6 mo. in treatment for enlarged thymus (treated 1926-1957; follow-up in 1963). Hempelmann et al., 1967	13-38	61-600	Lower dose group 2,207 (32,226 person yr at risk)[f]	Thyroid	4	0.07
				Thyroid (benign)	6	.80
				Leukemia	3	1.45
			Higher dose group: 498 (11,485 person yr at risk)	Thyroid	14	.06
				Thyroid (benign)	15	.60
				Leukemia	3	.57
8. Infants irradiated routinely with x-rays to anterior mediastinum through small (4 X 4 cm) port, 7 days after birth, as "apparently harmless and perhaps beneficial procedure" (x-ray 1938-46, follow-up 1956-58). Cooti et al., 1960	10-20	75-450 mostly 150	1,401, including 244 with enlarged thymus	Thyroid carcinoma	0	0.03
				Leukemia	0	0.95
9. Children treated with x-rays to head, neck, or chest for various benign conditions, mainly "enlarged" thymus and adenitis, treated before age 16 and followed till age 23. Saenger et al., 1960	>11 (83%)	<50 (4%) 50-200 (36%) 200-600 (33%)	1,644	Thyroid	11	0
				Thyroid (benign)	7	0
10. Children treated before age 16 with x-rays for enlarged thymus, pertussis, and head and neck diseases; and died before age 23 (treated 1930-1956; follow-up 1940-1956). Murray et al., 1959	Up to 23	Not given	3,872	Leukemia	7	1.4
11. Patients (most between ages 10-40) treated with x-rays for benign lesions in neck, mainly for tuberculous adenitis (treated between 1920-50). Henford et. al., 1962	10-40	100-2000	295	Thyroid	8	0.1
12. Patients, ages 20-70, treated with x-rays to thyroid for benign disorders. DeLawter and Winship, 1963	10-35	1500-2000	222	Thyroid	0	
13. Hyperthyroid patients treated with ^{131}I (treated 1946-64; follow-up through June 1967). Saenger et al., 1968	3-21	7-15 rads to bone marrow (9 mCi ^{131}I av.)	18,370 (119,000 person yr at risk)	Leukemia	17	11.9

Table 1 (Continued)

Subject of study	Follow-up time (yr)	Dose (R or rads)	No. of persons[a]	Form of cancer	No. of cases: Observed in exposed group[b]	No. of cases: Expected if not exposed[c]
Comparison group treated by surgery and not given ^{131}I. Saenger et al., 1968			10,731 (114,000 person yr at risk)	Leukemia	16	11.4
14. Hyperthyroid patients, ages 20-60, treated with x-rays (treated 1946–53; follow-up 1959-61). Sheline et al., 1962	5-15	Not given	182	Thyroid (probable) Multiple benign thyroid nodules	1 7	
15. Patients treated with x-rays to spine for ankylosing spondylitis (treated 1935–54; follow-up to Jan. 1963). Court Brown and Doll, 1965	5-28	250-2500 to spinal marrow; approx. 7% of spinal dose to other sensitive areas	14,302 (165,631 man yr at risk)	Leukemia Aplastic anemia Cancer of heavily irradiated sites (after 6 yr)	60 16 200	6.8 .61 107
16. Patients treated with x-rays for cancer of the cervix. Hutchison, 1968	4-8 (31%) <4 (69%)	300-1500 av., to bone marrow	27,793 (57,121 person yr)	Leukemia Lymphatic malignancy	4 6	5.1 6.3
17. American radiologists (died 1948–1964). Lewis, 1970	Through 1964		530 deaths	Leukemia Multiple myeloma Aplastic anemia	13 5 5	3.91 1.01 .23
18. American radiologists. Warren and Lombard, 1966.	Through 1960		5,982	Leukemia 1940–44 1945–49 1950–54 1955–60	 4 7 6 7	 0.5 .86 1.26 2.05
19. American radiologists. Seltser and Sartwell, 1965	1935–58		3,521 (48,895 person yr)	Ages 35-49 Leukemia Other cancer Total deaths Ages 50-64 Leukemia Other cancer Total deaths Ages 65-79 Leukemia Other cancer Total deaths	 2 9 79 8 54 339 9 72 438	 1.9 7.3 61.5 1.1 32 271.5 4.7 48 295
20. Radium dial painters and others who ingested radium and thorium. Evans, 1967	More than 40		420	Bone	No significant clinical signs of malignancies for body burdens <0.5 μCi ^{226}Ra	
21. Uranium miners exposed to radon gas and decay products; follow-up 1950–63. Wagoner et al., 1965.			3,415	Lung	22	5.7

[a]This refers to the number of individuals at risk unless otherwise specified.

[b]The information needed to determine the number of cases is obtained by either following a designated study population or by working back from a review of all death certificates in a defined geographical area.

[c]The numbers in this column are based on available statistical data for unexposed populations.

[d]The term person-rads pertains to the dose imparted to a population and is equal to the sum of the doses incurred by the individuals in the population.

[e]This figure is based on a systematic sampling of the population rather than a review of all the records.

[f]The term person years at risk is the sum of the number of years in which the disease could develop in each member of the group.

4. Genetic effects (genetic abnormalities transmitted to future generations) are known to occur in experimental studies on short-lived animals. Although similar genetic changes may also be induced in humans, none have yet been demonstrated (even in the Japanese survivors who received considerable radiation dose). Scientists calculate the probability of increase in genetic mutation due to radiation by using the concept of doubling dose (dose of radiation required to produce a number of mutations equal to those which occur naturally). The doubling dose for chronic radiation of human populations is estimated to fall in the range of 20-200 rems.

III. LOW DOSE EFFECTS

The radiation effects on human populations exposed to less than 5 rems are difficult to demonstrate and quantify. The literature contains many studies which have attempted to demonstrate differences between low level irradiated and non-irradiated equivalent populations. The results are suggestive but often fall short of being conclusive, due to inherent methodological problems. These problems are related to 1) lack of accurate dosimetry, 2) difficulty of having exactly equivalent control populations, 3) isolation of radiation effects from similar effects due to other physical or chemical agents, 4) deducing cause-effect relationship when there is a long latent period (up to 30 years) between the time of exposure and the time when effect occurs, 5) repair of sublethal damage, 6) time over which radiation is accumulated and age of persons at risk, 7) synergistic effects in presence of factors like hormones or other chemicals, 8) smallness of the effect compounded by smallness of the sample size studied and 9) the impossibility of repeating the observation for scientific verification.

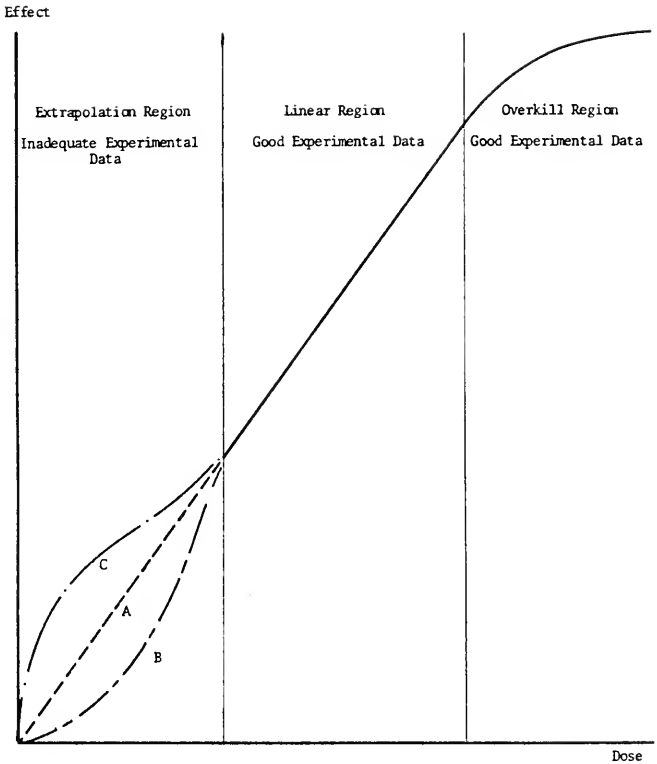
For human populations, it is, therefore, customary to estimate low dose radiation effects on the basis of known high dose effects. The most widely publicized estimates have been made by prestigious scientific groups such as the Committee on Biological Effects of Ionizing Radiation (BEIR Committee), National Academy of Sciences, 1972) and the United Nations Scientific Committee on Effects of Atomic Radiation (UNSCEAR 1972 & 1977). In extrapolating risks for doses below the range of measured effects, certain assumptions and hypotheses have been required. Generally, assumptions have been used which err on the side of caution and safety. These assumptions, which are considered theoretically sound and viewed as over-estimating the probable effect, are:

1. That there is no threshold dose below which radiation exposure is harmless.

2. That all radiation effect is additive without repair.

3. That the effect at low doses is proportional to the response at high doses (linear hypothesis).

Estimates of risk based on these assumptions are said to be derived from the "Non-Threshold Linear Hypothesis" and follow the dose response Curve A in Figure 1.



Curve A: Linear Extrapolation
Curve B: Linear Quadratic Extrapolation
Curve C: Supra Linear Extrapolation

Figure 1: Possible Shapes of Dose Response Curve

Two other dose response hypotheses considered as possible alternatives for the linear hypothesis are the "Linear Quadratic Hypothesis" and the "Supra Linear Hypothesis".

The linear quadratic dose response (Curve B, Figure 1) suggests that the radiation risk per rem is less at low doses, perhaps because low doses permit cells to more readily repair sublethal damage. Some scientists believe theory and experiment show the linear quadratic model to be superior to the linear model.

A few investigations, particularly those from the Hanford and Tri-State Studies, report low level radiation leading to cancer incidences far in excess of those expected from the above theories. If such incidences are proven to result from radiation alone, we would require a radical change in our present theories. The Science Work Group of the HEW Interagency Task Force on Ionizing Radiation recently concluded that these studies are suggestive of higher risks and a 'Supra linear' dose response (Curve C, Figure 1); but none of the studies were deemed sufficiently extensive, complete, or free from methodological complications to provide conclusive justification for altering our present concepts.

In this seminar, we will hear a lot about these alternative hypotheses, their implications, and the confidence limits on our probability estimates of low level radiation risks.

Changes Due to Energy Transfer from Radiation to Living Cells

The principal means by which radiation transmits energy to matter it traverses is by 'ionization' (i.e., removal of orbital electrons) and less importantly 'excitation' (i.e., moving normal orbital electrons to their excited states). Ionization and excitation of cellular molecules is referred to as "Direct Action" and can result in cell death, loss of reproductive capacity, gene mutation and other biological effects.

In addition, there is 'Indirect Action', where the irradiation of water in cells results in reproduction of highly reactive $\dot{H}$ and $\dot{O}H$ radicals and other products which in turn chemically react with cellular molecules to produce effects similar to those from direct action.

The cellular damage is roughly proportional to the energy absorbed from the radiation. Some of the cellular changes, however, are only temporary and recovery of sublethal damage occurs within a few hours after irradiation. The extent of recovery depends on the extent or type of damage, the total radiation dose, the rate at which radiation is delivered and the environment of the cell. This phenomenon of recovery is believed to play an important role in the ultimate effect on the organ or body as a whole. However, to be on the cautious side, no allowance is usually made in calculations of population risks.

The acute somatic effects are related mostly to cell death and occur at high doses above about 100 rems. Late somatic effects, developmental effects

and genetic effects are related mostly to sublethal molecular changes and mutations. These can, therefore, occur at low doses. Such changes can also remain dormant over a long latent period (10-30 years) or, in fact, never become apparent over a person's lifetime. Some of the genetic mutations can, however, be transmitted to the progeny of the irradiated parents.

Genetic mutations are constantly occurring at a definite, but very low rate, due to natural causes. Natural selection tends to eliminate harmful genes from the population but they are again replenished by new mutations, so that a general state of equilibrium exists. The concern is that man made causes, like chemicals or radiation, may unduly alter this equilibrium state.

Sources of Radiation Exposure to Man

Sources of radiation may be divided into Natural and Manmade.

NATURAL SOURCES:

Natural sources include: cosmic rays, natural radioactive materials in the earth, building materials and the human body itself. The contribution from terrestrial radioactivity is around 60 mrem/yr per person. The contribution of cosimc rays is 40 mrems/yr near sea level but increases at higher altitudes. In Denver, natural external radiation exposure levels are 114-188 mrems, in New York City, 87 mrems.

Naturally occurring radionuclides, like Potassium 40, Carbon-14, Hydrogen-3, are also incorporated in the body. In addition, radioactive noble gasses (radon and thoron) are produced by decay of uranium and thorium in the earth. We constantly breathe minute traces of these gasses and their radioactive daughters (polonium, lead and bismuth). These substances form an internal source of radiation exposure to the extent of about 30 mrems/yr.

MANMADE SOURCES:

Manmade sources of radiation contribute additional human exposure which is not as uniformly distributed throughout the population. The largest contribution in this category comes from medical and dental radiography. The genetically significant dose to the U.S. population from this source is around 55 mrems per person per year. It must be recognized, though, that this deliberate use of radiation does not involve the entire body and is associated with a definite benefit to human health. Its use is based on considerations of benefit-risk analysis.

In addition, nuclear weapons tests, nuclear power plants, uranium mining and fuel reprocessing plants all contribute to increased radioactivity in the environment. The exposure to humans, due to these sources, is normally around 4 mrems/year. These sources do, however, add considerably higher exposures to radiation workers. Again, the use of these technologies must be based on benefit-risk considerations. Accidental releases of radioactivity from these sources should be a major societal concern and warrant preventive measures, expenditures and legislation to minimize these risks.

In summary, the population exposure from both natural and manmade sources of radiation under normal conditions is between 100-200 mrems/yr per person depending on location, altitude, number of diagnostic tests, etc. Except for the newly introduced diagnostic radiation, man has survived this low level exposure for millenia.

Exposures from the Three Mile Island incident have been reported to be no more than 80 to 130 mrems within two or three miles of the plant. The average is less than 1 mrem beyond ten miles. The additional exposures from radioactive isotopes (mainly Iodine-131, Strontium-90 and Cesium-137) depend upon extent of ingestion. The most important of these elements, Iodine-131, was detected at levels of 41 picocuries/litre of milk from the region. Up to 300 picocuries/litre were detected in this same Pennsylvania milk following the Chinese nuclear test. The FDA requires action to be taken when the iodine content reaches 12,000 picocuries/litre of milk. The relative levels of exposure from different sources and their significance is presented in Table 2. The probabilities of particular effects occurring after 1 rem exposure are given in Table 3.

The seminar presented comprehensive information on what is known about the extent of radiation exposure and the expected risks.

This introductory overview was prepared only to give background information as an aid to understanding material presented in the seminar. The tables and data reproduced here were not specifically calculated for the TMI incident and must be used as broad guidelines.

REFERENCES

1. The Effects on Populations of Exposure to Low Levels of Ionizing Radiation, (BEIR report). National Academy of Sciences, National Research Council, Washington, DC, November 1972.

2. Sources and Effects of Ionizing Radiation, UNSCEAR Report, United Nations, New York, 1977.

3. 'Radiation Protection', by Jacob Shapiro, Harvard University Press, 4th Printing 1978.

4. 'Physical Foundations of Radiology', by Goodwin, Quimby and Morgan, Harper and Row 1970.

5. Work Group Reports of HEW Interagency Task Force on Ionizing Radiation, Department of HEW, February 1979.

Table 2

Significance of External Radiation Levels

Exposure	Significance
I	
22 mR/calendar quarter, continuous whole body (0.011 mR/hr)	Background radiation, sea level, out of doors, New York City
41 mR/calendar quarter, continuous whole body	Background radiation altitude of 10,000 ft (ground level)
34 mR/calendar quarter, cootinuous whole body	Radiation measured inside brick building at sea level
2200 mR/calendar quarter, cootinuous whole body	Exposure at cruising altitude of supersonic transport (60,000 ft)
II	
1250 mrem/quarter	Limit for occupational exposure of whole body (critical organs are gonads, lens of eye, and bone marrow)
18,750 mrem/quarter	Limit for occupational exposure of hands
125 mrem/quarter	Limit for nonoccupational exposure (including exposure of minors)
15,000 mrem/year	Single tissue or organ limit if not covered in separate recommendation.
III	
<2 mrem in an hour and <100 mrem in any 7 consecutive days	Unrestricted area. No control or sign required
>2 mrem in an hour or >100 mrem in any 7 consecutive days	Control of area required
>5 mrem in 1 hour to major portion of body	Radiation area sign required
>100 mrem in 5 days to major portion of body	Radiation area sign required
>100 mrem in 1 hour to major portion of body	High radiation area sign required
IV	
1 R, major portion of bone marrow	Risk of occurrence of leukemia is about 1 in 50,000
1 R, sensitive organ	Risk of eventual appearance of cancer about 1 in 50,000
10 R, whole body	Elevated number of chromosome aberrations in peripheral blood; no detectable injury or symptoms
20 R, reproductive system	Dose for doubling spontaneous mutations (lowest of proposed values)
100 R, single dose, whole body	Mild irradiation sickness
650 R, single dose, whole body	Approximately 50% will not survive even with best care
400–500 R, low energy x-ray, local	Temporary loss of hair
500–600 R, single dose, locally to skin, 200 keV	Threshold erythema in 7–10 days, followed by gradual repair, dryness and dull tanning.
2000 R locally to skin from 1 MeV x-ray at 300 R/day	Threshold erythema
600–900 R, locally to eye	Radiation cataract
1,000–2,500 R, local, at 200–300 R/day	Treatment of markedly radiosensitive cancer
1,500–2,000 R to skin, single dose, 200 keV	Erythema, blistering, residual smooth soft depressed scar
2,500–6,000 R, local, at 200–300 R/day	Treatment of a moderately radiosensitive cancer
V	
700–1,380 mR[a]	Mean exposure per dental film per examination in 15–29 yr age group (1964)
45 mR[b]	Mean exposure per chest x-ray (radiographic, 1964)
500 mR	Mean exposure per chest x-ray (photofluorographic, 1964)
5,000 mR/min[c]	Output from properly operating fluoroscope without image intensifier

[a] 400 mR and less per exposure practical (1968).
[b] 10–20 mR practical (1968).
[c] less than 2,000 mR/min with image intensifiers.

Table 3

Risks of Various Consequences of Exposure to 1 rad of Radiation

Consequence	Risk
a. Cancer resulting from irradiation of adults	
Bone marrow (leukemia)	1/50,000
Thyroid	1/50,000
Pharynx	1/50,000
Bronchi	1/50,000
Stomach	1/50,000
Pancreas	1/50,000
Large intestine	1/50,000
b. Cancer in childhood from irradiation of fetus	1/2,500
c. Genetic consequences from irradiation of gonads	
Mutation resulting in genetic death in generation immediately following exposure	1/10,000
Mutation resulting in marked genetic detriment to live children (dominant mutation)	1/100,000
d. Genetic deaths following exposure of a parental generation of one million persons to 1 rad	
During following 10 generations[a]	2000
To infinity	8500

Sources: Data supplied in ICRP, 1966, Report 9 and ICRP, 1969, Report 14. The genetic risks in (c) are estimated for exposure of one parent only by multiplying estimates from ICRP, 1966, Table 16, by 1/2.

[a]ICRP, 1966, p. 57, par. 3.3. The natural level is 1000 times as high, or 2,000,000 (in 10 generations) compared to 2,000 from 1 rad of radiation.

Note: These risk values should be taken only as crude and probably conservative estimates which are useful for assessment of radiation control measures.

THE TMI RADIATION DOSIMETRY AND EARLY HEALTH IMPLICATIONS

Niel Wald, M.D.

It is a privilege to open this seminar. Hopefully, it will fulfill its purpose of familiarizing physicians with the realities of the Three Mile Island nuclear station incident of the 28th of March and its succeeding events, and give you a basis for providing reasonable and meaningful answers to your patients and, perhaps, to your communities when questions are raised about the health implications of this incident.

What I will present first is information concerning the radiation exposure assessment which was developed by many groups, and which I collected in part in my role as an advisor to Dr. Gordon MacLeod, the Pennsylvania Secretary of Health, the State Health Department and the Governor's office, beginning a couple of days after this incident began and its problems began to manifest themselves.

It is important for the purpose of radiation medicine, i.e., the diagnosis and treatment, and, hopefully, prevention of radiation injury, to have some idea about the nature of the radiation exposure. Radiation medicine differs from most medical specialties. The orthopedic specialist does not know the pounds of peak overpressure that an ankle bone sustained; the physician in infectious diseases does not know the number of bacteria to which the individual has been exposed. We approach things differently in this esoteric medical specialty because we do much of our diagnostic work and draw many conclusions on the basis of exposure information. We have an advantage, perhaps a luxury, in that there exists technology to determine very accurately the exposure involved in many of the accidental situations for which our help is asked.

There is another side of the coin. A lot of alarm is aroused on the part of people who are not familiar with radiation dose measurements, their meaning, and their biological implications. Because the unusual fact that we have this information, such people, who may be anxious anyway, tend to consider that its very existence itself is a bad sign.

What I will try and do, then, is to provide some perspective on the exposure situation based on this incident, which will then provide a frame of reference, perhaps, for consideration of the early health effects to which I will address myself briefly, and also for the long-term health effects which the other members of the panel will consider.

The basis for the radiation exposure information to be presented is primarily work done by a number of groups; the Bureau of Radiation Protection of our Pennsylvania State Department of Environmental Resources, as well as the Pennsylvania State Health Department; the Nuclear Regulatory Commission;

the Environmental Protection Agency and the Department of Health, Education and Welfare, including both its Center for Disease Control and its Food and Drug Administration.[1] The prompt turnout and the responsible and complete manner in which these groups cooperated in assessing the exposure was noteworthy. The information is still preliminary in the sense that improvements in analysis are always possible and are continually being made. There will be, as the time lengthens, increasing refinements that will be made to these numbers, but what I will give you is certainly a reasonably good estimate on most of the findings and they will not change drastically to the extent of altering the health conclusions.

Just to set the stage, Figure 1 shows something that everyone has obviously seen who has read a newspaper or magazine within the last few weeks --the Three Mile Island plant and its geographic environs. I want to call your attention to the circles, which define the different circumferences from the point of release of radiation exposure--5 miles, 10 miles, 20 and 25 miles. Of course, the population increases along with these increasing areas.

It is important to have some idea of the population distribution in this area, as shown in Figure 2. In talking about the health effects, if there is nobody there, there is no health problem. You can see that there are certain areas defined in the segmental approach here, in which the population is less than in others. Depending on which wind direction was prevailing during a brief gaseous release of radioactivity, the population of the involved sector will determine the significance of that release. Some of the dosimetric studies involved assessment, hour-by-hour, of wind direction in order to estimate exposure, not blindly by distance from the plant, but in terms of which way the radioactivity was really going and how many people were there.

Let's consider the source of the exposure first, as seen in Figure 3. I do not plan to review the mechanics of the accident. The important thing from our standpoint has to do with where and what radioactivity was released. Figure 4 shows a plan which identifies the reactor building for Unit #2 and an auxiliary building. The auxiliary building became the location of a lot of excess radioactive water from the reactor containment. It had not been designed to contain radioactive material and this, then became the point of release of radioactive gases, predominantly ^{133}Xe and some ^{131}I.

Note, just for geographic orientation, that across the river is what has become known as Trailer City, which was originally the observation facility that the company had set up so people could see the local power plant. It grew as the various federal agencies and state agency and other working groups moved in to help with the mechanics of the problem. A lot of the measurements were made in the Trailer City area and that is why I point it out to you.

1. This work was subsequently reported as "Population Dose and Health Impact of the Accident at the Three Mile Island Nuclear Station" (a preliminary assessment for the period March 28 through April 7, 1979), by the Ad Hoc Population Dose Assessment Group consisting of Battist, L. (NRC), Buchanan, J. (NRC), Congel, F. (NRC), Nelson, C. (EPA), Nelson, M. (HEW), Peterson, H. (NRC) and Rosenstein, M. (HEW) May 10, 1979. The report is for sale as Stock Number 017-001-00408, Supt. of Documents, Government Printing Office, Washington, DC 20402.

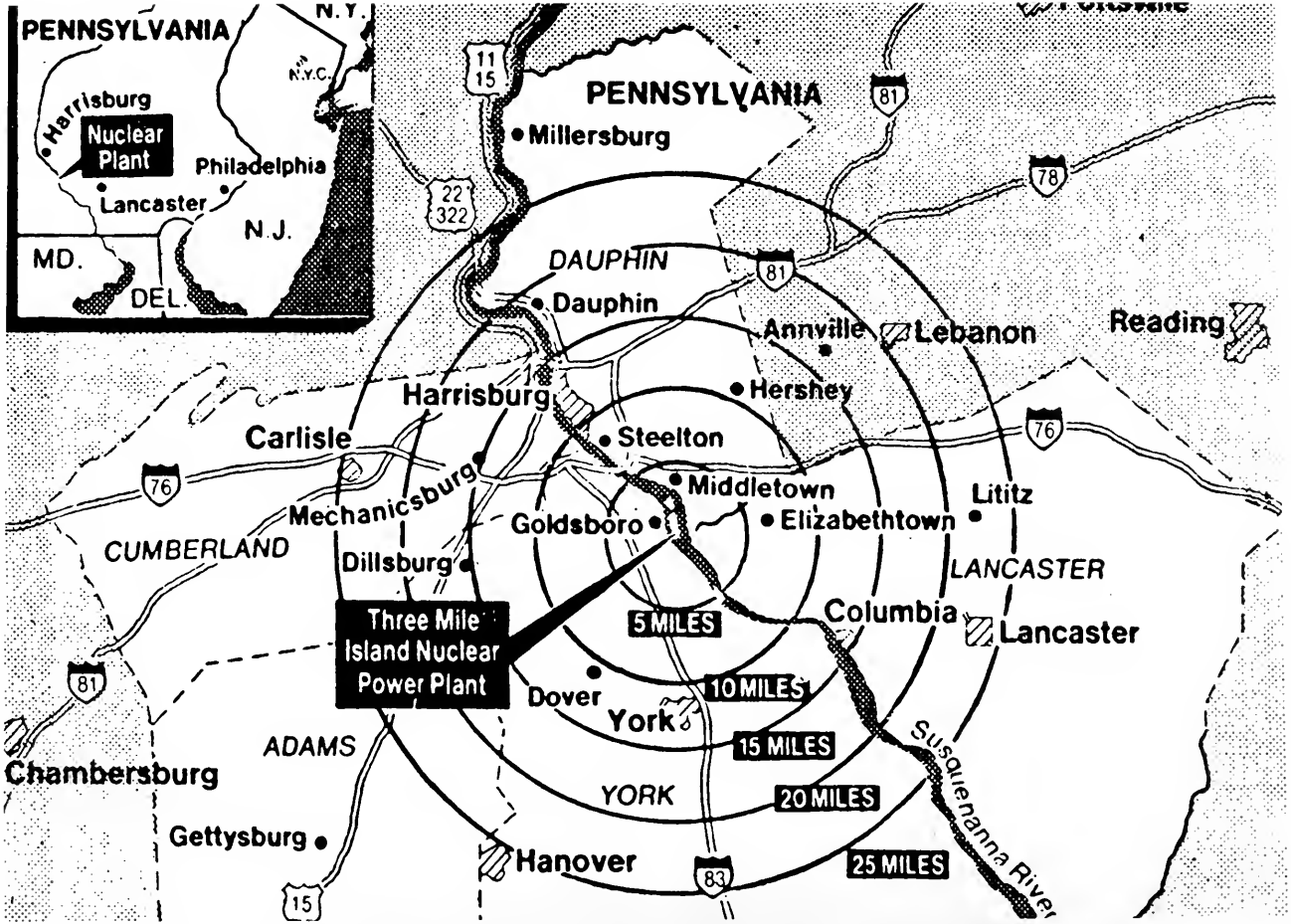


Figure 1: Geographic environment of Three Mile Island

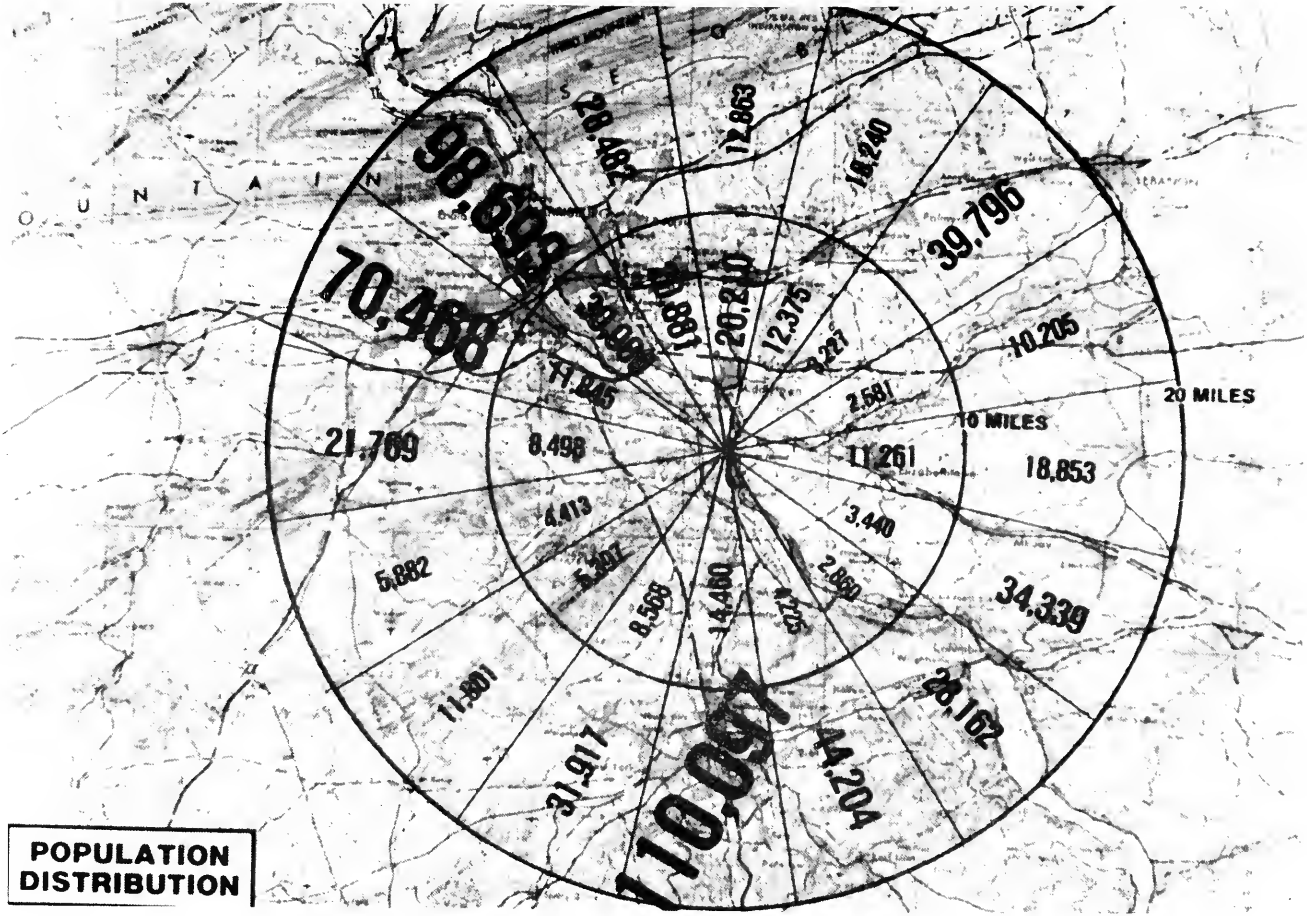


Figure 2: Population distribution near TMI

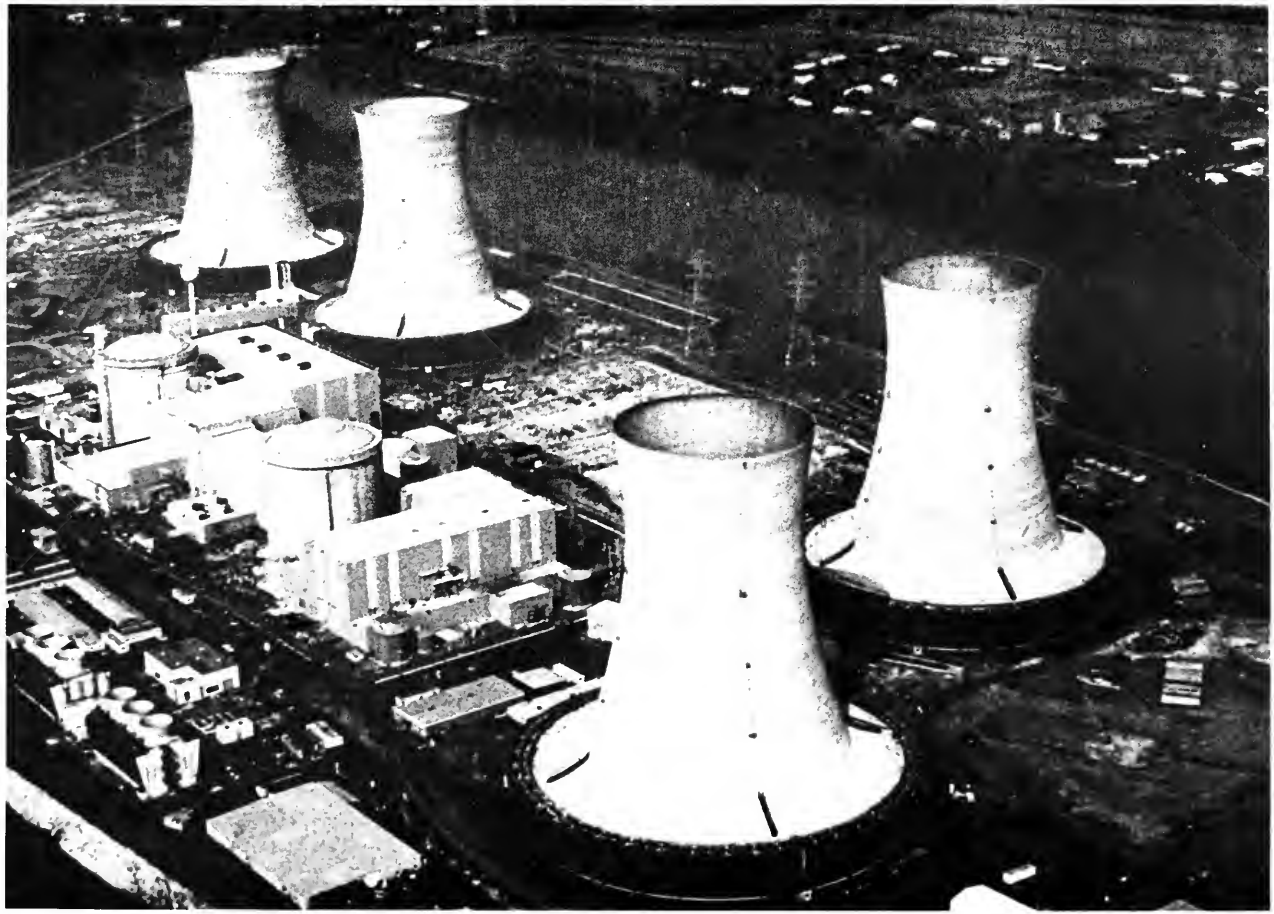


Figure 3: The TMI reactor plant

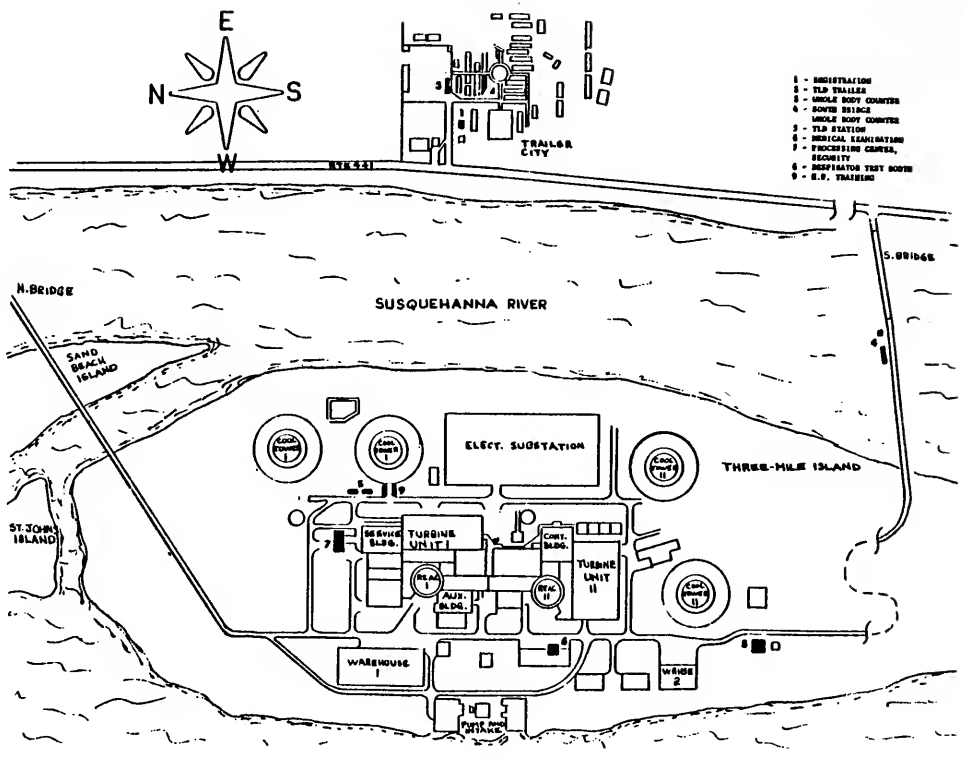


Figure 4: Plan of the reactor and auxiliary buildings

The effort to define the exposure was carried out in a number of different ways, and one of the most important was based on the thermoluminescent dosimeters or so-called TLD's. The TLD's are solid radiation detectors made of calcium or lithium fluoride crystals. They respond continually to the exposure they are receiving and so give a cumulative reading. The interpretation of the TLD results depends on where the TLD's were placed as shown in Fig. 5 and how long they were there.

Initially, the TLD's in place were the ones that the State puts around all reactor facilities in the State for surveillance purposes, plus the ones placed by Metropolitan Edison, the company that runs the reactor. These were added to by the State and by the FDA (Federal Drug Administration), the EPA (Environmental Protection Agency) and the NRC (Nuclear Regulatory Commission). The results that I will give you, then, are based on the TLD dosimeters which were put in place by all of those groups.

Table 1 presents the estimated radiation dose which is a "worse case" example because it is based on where the plume of radioactive gases was going, containing particularly the Xenon-133 which was the main source of radiation, although there was some traces of Iodine 131 along with it. The time period of the radiation releases from the incident is defined here, and you can see that most of the exposure occurred in the first three days. As filter changes were taking place to control the venting from the auxiliary building, there were additional puffs of exposure. This hypothetical "worse case individual" is located one-half mile from the stack and this is where the most radioactivity would have landed. If he stayed outdoors over this entire time, the total cumulative exposure estimate based on the TLD dosimetry is about 86 millirem.

In terms of magnitude of exposure, it is useful to compare this exposure to such things as the cosmic and terrestrial radiation, which is part of our natural radiation backgrounds, as shown in Table 2. There is a lot of variation, so that places at high altitude differ from those at sea level and places where there is a lot of granite are different than places where there is none. Rocky areas like Denver, CO have more terrestrial radiation than desert areas like Las Vegas, NV. Similarly, cosmic radiation in high-altitude places is higher than in low-altitude places.

Table 3 shows a difference of about 80 millirem, for instance, if you compare Denver to Harrisburg. This is a natural difference that people are exposed to year-in, year-out, living at higher altitude versus lower. Even living in a brick house rather than a wooden-frame house makes about a 14 millirem difference. There are also sex differences because of the amount of potassium, which is present in all of us, part of it being radioactive since the world began. These differences add up to the same order of magnitude as the 86 millirem hypothetical highest exposure person at TMI compared to somebody not exposed.

If you take the average dose to a typical individual within 10 miles of the site or within 50 miles of the site, as shown in Table 4, you can see that for about 160,000 people in that 10-mile range, 11 millirem is the average dose, or 1.6 millirem, if you take the two million people within the 50-mile range. Comparing these to the 86 millirem for the worse case individual, you can see

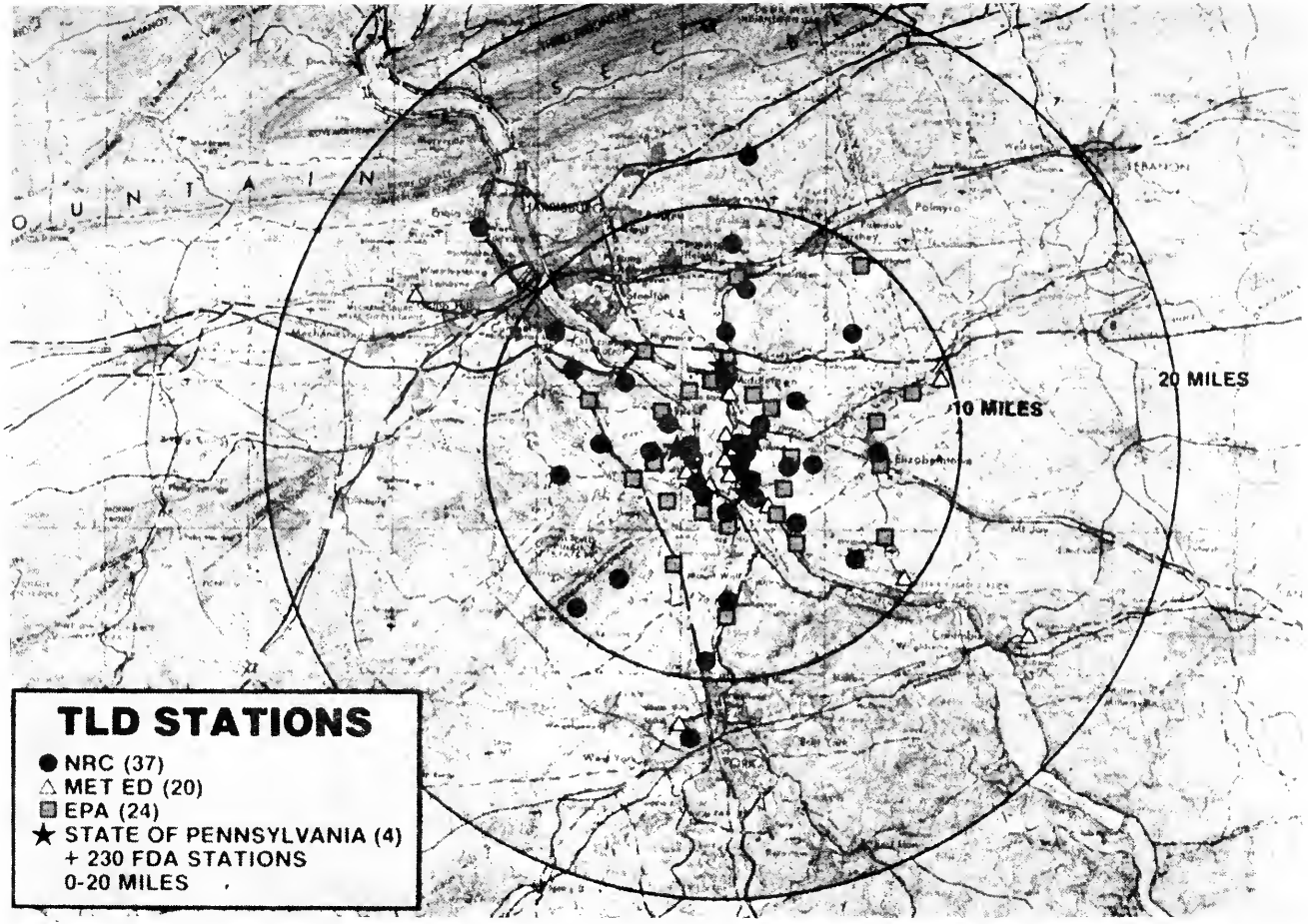


Figure 5: Distribution of thermoluminescent dosimeters

Table 1

ESTIMATED MAXIMUM DOSE TO AN INDIVIDUAL
(Located east or northeast of the site)

Period (1979)	Estimated Dose (mrem)	Cumulative Total dose (mrem) (to nearest mrem)
3/28 - 3/29	45	45
3/29 - 3/31	29	74
3/31 - 4/1	8	82
4/1 - 4/2	0	82
4/2 - 4/3	1	83
4/3 - 4/4	0	83
4/4 - 4/5	1	84
4/5 - 4/6	2	86
4/6 - 4/7	0	86

Table 2

Estimates of Natural "Background" Radiation Levels in the United States

Location	Annual Dose Rate (mrem/year)			
	Cosmic Radiation[a]	Terrestrial Radiation[a]	Internal Radiation[b]	Total
Atlanta, Georgia	44.7	57.2	28	130
Denver, Colorado	74.9	89.7	28	193
HARRISBURG, PA.	42.0	45.6	28	116*
Las Vegas, Nev.	49.6	19.9	28	98
New York, NY	41.0	45.6	28	115
PENNSYLVANIA	42.6[c]	36.2[c]	28	107
Washington, DC	41.3	35.4	28	105
UNITED STATES	40-160	0-120	28	70-310

Table 3

Comparison of Individual Doses from the Three Mile Island Accident With Variations in Natural Background Radiation Doses

NATURAL BACKGROUND VARIATION	ESTIMATED DIFFERENCE IN ANNUAL DOSES
Living in Denver, Colorado compared to Harrisburg, PA (from Table 4-4)	+ 80 mrem/yr
Living in a brick house instead of a frame house [Yeates data in (4) Table 16, p. 35]	+ 14 mrem/yr
Added dose from potassium-40 due to being male instead of female (There is 25% less potassium in women than men [(5), p. 106])	+ 4.8 mrem/yr

Table 4

Comparison of Individual Doses from the Three Mile Island Accident With Variations in Natural Background Radiation Doses

Source of Radiation Exposure	CUMULATIVE TOTAL BODY DOSES DELIVERED THRU 4/7/79
THREE MILE ISLAND ACCIDENT	
Individual remaining out-of-doors at location of highest estimated offsite dose	86 mrem
Average dose to a typical individual within:	
50 miles of site	1.6 mrem
10 miles of the site	11 mrem

that these differences are comparable to natural differences that we, as an earthdwelling species, have lived with for a long time.

If you cumulate the exposure to the total population with an area, you arrive at a unit called 'person-rem', which is used in talking about cumulative or collective dose. This is based on a concept that says that the average exposure times the number of people is the person-rem exposure. As presented in Table 5, the 0 to 10-mile person-rem estimate for the first nine days is about 2,000. The 10 to 50 mile exposure is a little bit less, if you take the cumulative person-rem estimate for the population of about two million within 50 miles over the first couple of weeks.

This is a cumulative population exposure, if you will, which is a basis for prognostication about late effects in the population, and I show it to you for that reason. The estimate has been modified from some even earlier data by the addition of more TLD information, and that has refined it to the present state. It probably will be refined further, and it might be 4,000 person-rems rather than 3,500 as further investigation proceeds. But that is a ball-park figure. This estimate is based entirely on the TLD studies.

Another approach to the assessment of the population exposure is to see which way the wind is blowing and try to measure any radioactivity being released. Figure 6 shows the meteorological stations that were in place both on the surface and also in the upper air on high-altitude structures. To develop more information, the Nuclear Regulatory Commission brough in helicopters within 12 hours of the start of the incident that could measure radiation in flight and follow the plume from the plant stack. The population exposure can be determined using this technique independently of the TLD measurements. Figure 7 shows an example of both the noon and evening delineation of the magnitude and direction of the radioactivity plume on the 30th of March.

You can see that the dose rate right over the stack is 30 millirem per hour, but where the people are, the rate is 1/2 to 1 millirem per hour within the 10-mile zone and 1/10 to 2/10 of a millirem per hour in the 10 to 20 mile zone. This kind of estimate then can be refined considerably to estimate the cumulative population dose, based on exactly which way the wind is blowing, and an hour-by-hour computerized plotting of the estimated exposure using actual measurements from the air sampling. The cumulated exposure over the first week after the onset of the incident is shown in Figure 8.

What this approach provides is an independent check on the population exposure estimates based on the meteorological measurements. Again we have the population by distance and the average exposure estimated by how long the plume was over the particular section of the circle. At greater distances, these are extrapolated estimates because there were no measurements when the radiation levels were too low to detect.

Table 6 shows the cumulative exposure in person-rem, which is about 1,700 millirem in the first week. Table 7 shows that in the second week another 50 millirem or so was added. These results, although obtained not by TLD's on the ground, but by the actual cloud-chasing measurements, sector-by-

Table 5

ESTIMATED COLLECTIVE DOSE (person-rem)

Period 1979	0-10 miles	10-50 miles	Total 0-50 miles	Cumulative Total, 0-50 miles (to nearest 50)
3/28-3/29	206	511	717	700
3/29-3/31	764	524	1288	2000
3/31-4/1	537	315	852	2850
4/1-4/2	44	35	79	2950*
4/2-4/3	109	133	242	3200
4/3-4/4	39	43	82	3260
4/4-4/5	49	82	131	3400
4/5-4/6	41	39	80	3450
4/6-4/7	42	35	77	3550**
	1831	1717	3548	

* In the original assessment, which formed the basis of testimony before the Senate Subcommittee on Health and Scientific Research, this value was estimated to be 1800.

** In updates of the original estimate, which formed the basis for testimony before the Senate Subcommittee on Nuclear Regulation, this value was estimated to be 2,500.

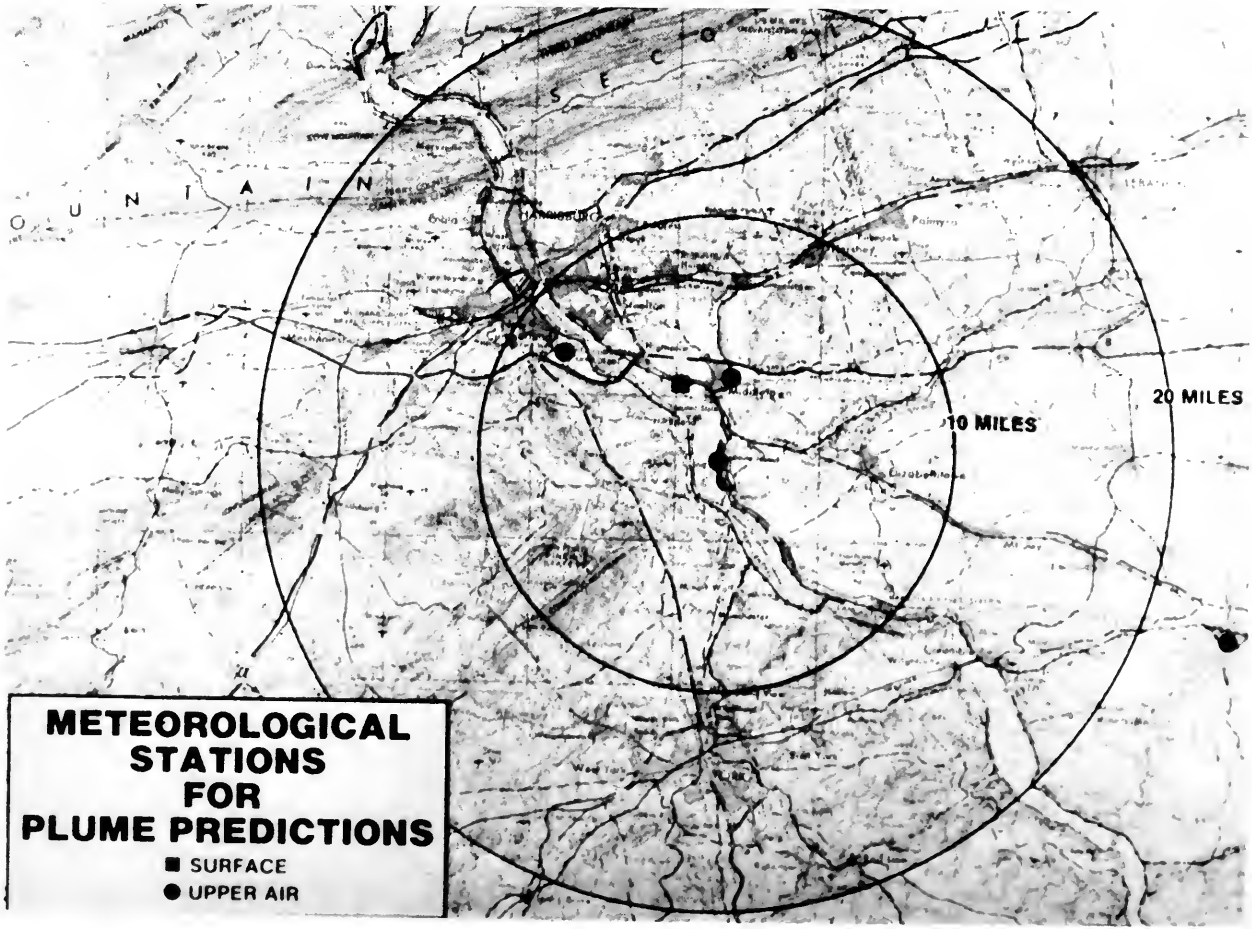


Figure 6: Surface and air meteorological stations

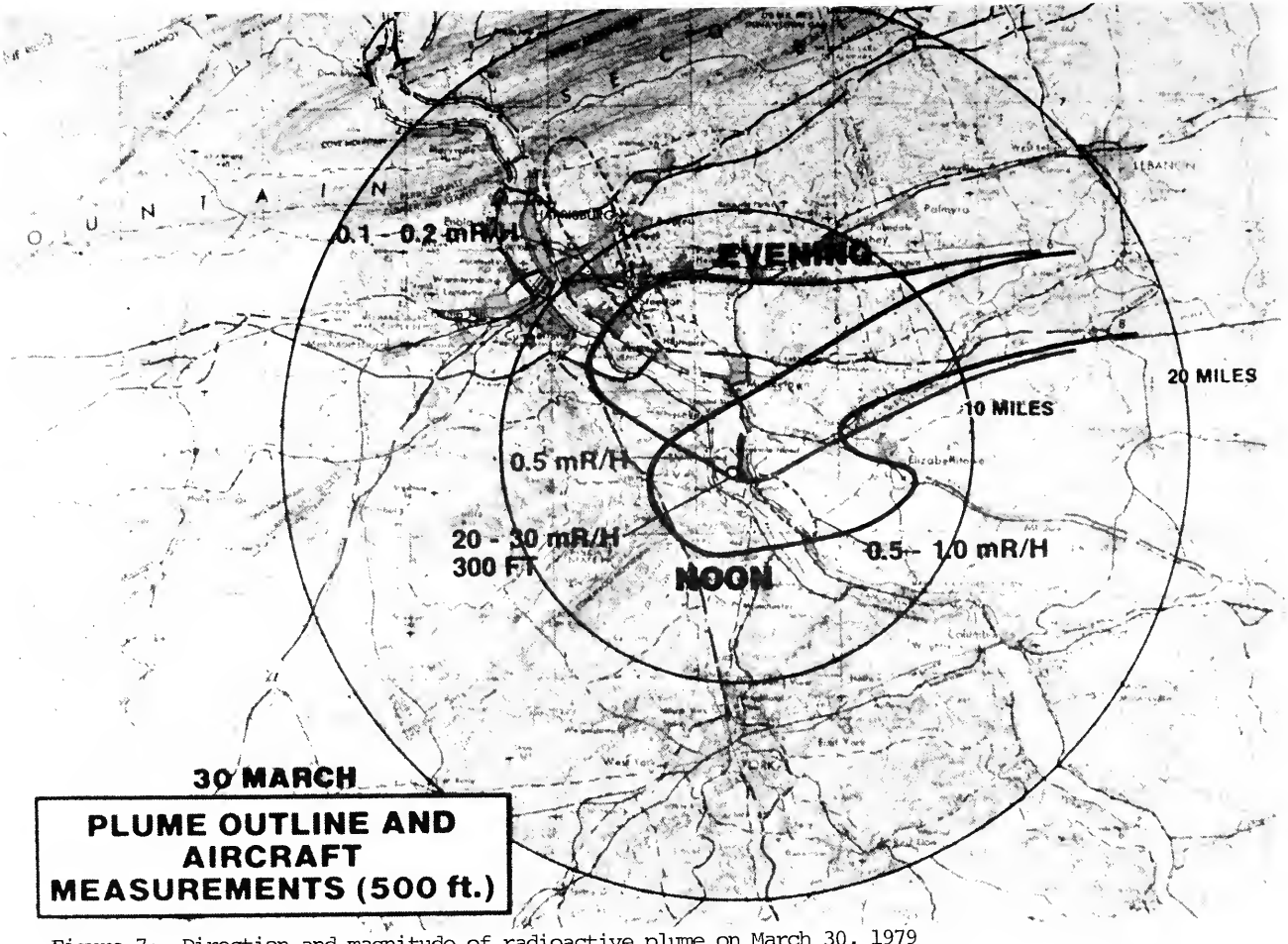


Figure 7: Direction and magnitude of radioactive plume on March 30, 1979

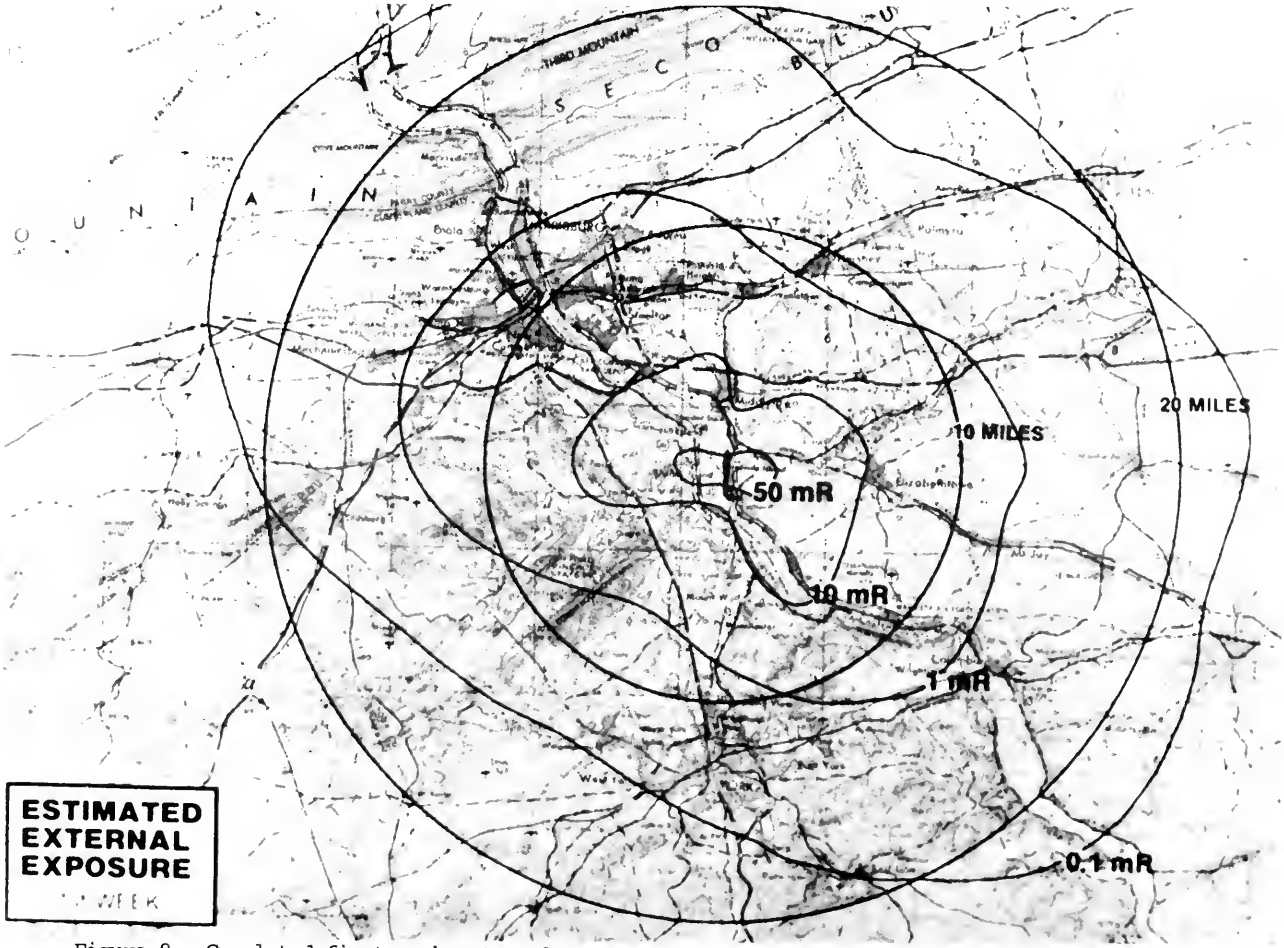


Figure 8: Cumulated first week external exposure

Table 6

3/28 - 4/3/79 Population Dose

Radius (Miles)	Exposure (Person-Rem)	Total Population	Individual Average Exposure (mr)
0- 1	29.3	658	45.0
1- 2	77.1	2,017	38.0
2- 3	208.4	7,579	27.0
3- 4	175.2	9,676	18.0
4- 5	132.9	8,891	15.0
5-10	780.7	137,474	5.7
10-20	258.2	577,288	0.45
20-30	14.1	433,001	0.033
30-40	0.64	273,857	0.0023
40-50	0.11	713,210	0.00015
TOTAL	1676.7±425	2,165,651	0.77

Estimated maximum exposure of hypothetical person 0.5 miles east of plant under plume 43 hours is 95±25 mr.

Table 7

4/4 - 4/10/79 Population Dose

Radius (Miles)	Exposure (Person-Rem)	Total Population	Individual Average Exposure (mr)
0- 1	1.09	658	1.65
1- 2	2.75	2,017	1.36
2- 3	4.10	7,579	0.54
3- 4	5.10	9,676	0.53
4- 5	2.96	8,791	0.34
5-10	20.30	137,474	0.15
10-20	9.91	577,288	0.017
20-30	0.13	433,001	0.0003
30-40	<0.01	273,857	<0.0002
40-50	<0.01	713,210	<0.0000002
TOTAL	46.34	2,165,651	0.021

sector, are in reasonable agreement with the TLD results.

There are other methods for looking for the released radioactivity other than these external measurements. The major concern about radio-iodine is that it gets into the body and the thyroid gland in particular. Airborne radio-iodine measurements were made early after the incident from various locations, shown in Figure 9 , in the TMI plant vicinity. You can see, in Table 8, that the highest reading was 20 picocuries per cubic meter in the air. There were some brief occasions when this was exceeded; for example, there was a one hour period during a plant filter change where there was a puff of 200 picocuries per cubic meter over Trailer City. The importance of this is that iodine gets into people and calculations were, therefore, made from the measured radio-iodine to estimate the possible dose to the thyroid over the first and second 3-day periods of the incident. The estimated exposure to the most sensitive organ of concern, which was considered to be the child's thyroid, was about 3 millirem, as shown on Table 9. This is a very low exposure which would not produce early effects and I will leave it for my colleagues to discuss any long-term effects later.

Another concern is the radioactive material getting into the environment where it may find its way to humans via the food chain. Evaluation of this possibility led to continuous monitoring of the environment at many locations in the area, shown in Figure 10. You can see the air, soil, water and vegetation sampling area which was being monitored in Figure 11. In some 400 or 500 environmental samples (water, vegetation and soil) which were collected during the first week and 850 by the end of the second week, there were only a couple of occasions of a trace amount on some vegetation.

Another question is....what is getting into people from the milk of cows grazing in the area? The dairy farms were located, as shown in Figure 12 and monitored. You have heard some of the results, or seen them in the newspaper, that indicated about 20 to 30 picocuries per liter in milk analyses. Many different agencies independently were making these measurements and a great overlap was found in the range of results. As shown in Table 10 , the range of positive results had an upper limit of 41 picocuries per liter, but the 41 picocurie result from FDA was later revised downward.

For comparison and for perspective, it should be recalled that the Chinese weapons tests gave us a 300 or 400 picocuries per liter two years ago in Pennsylvania. The action level that the Environmental Protection Agency sets, at which point one has to stop the milk from getting into distribution to consumers, is 1,200 picocuries per liter. So, again, these radioactivity levels are measurable but it doesn't necessarily mean that they are a public health problem, and, indeed, they weren't considered to be. I should add there was a market basket sampling going on also. In other words, the food and milk at the supermarket, in addition to raw milk samples at the dairies, were tested and there was no activity; no radio-iodine detected in any of the food or any milk.

How else can we corroborate or check on the validity of these kinds of measurements? Another way is to sample the exposed people. Whole body counting is a sensitive non-invasive technique for this purpose. It is simply a very

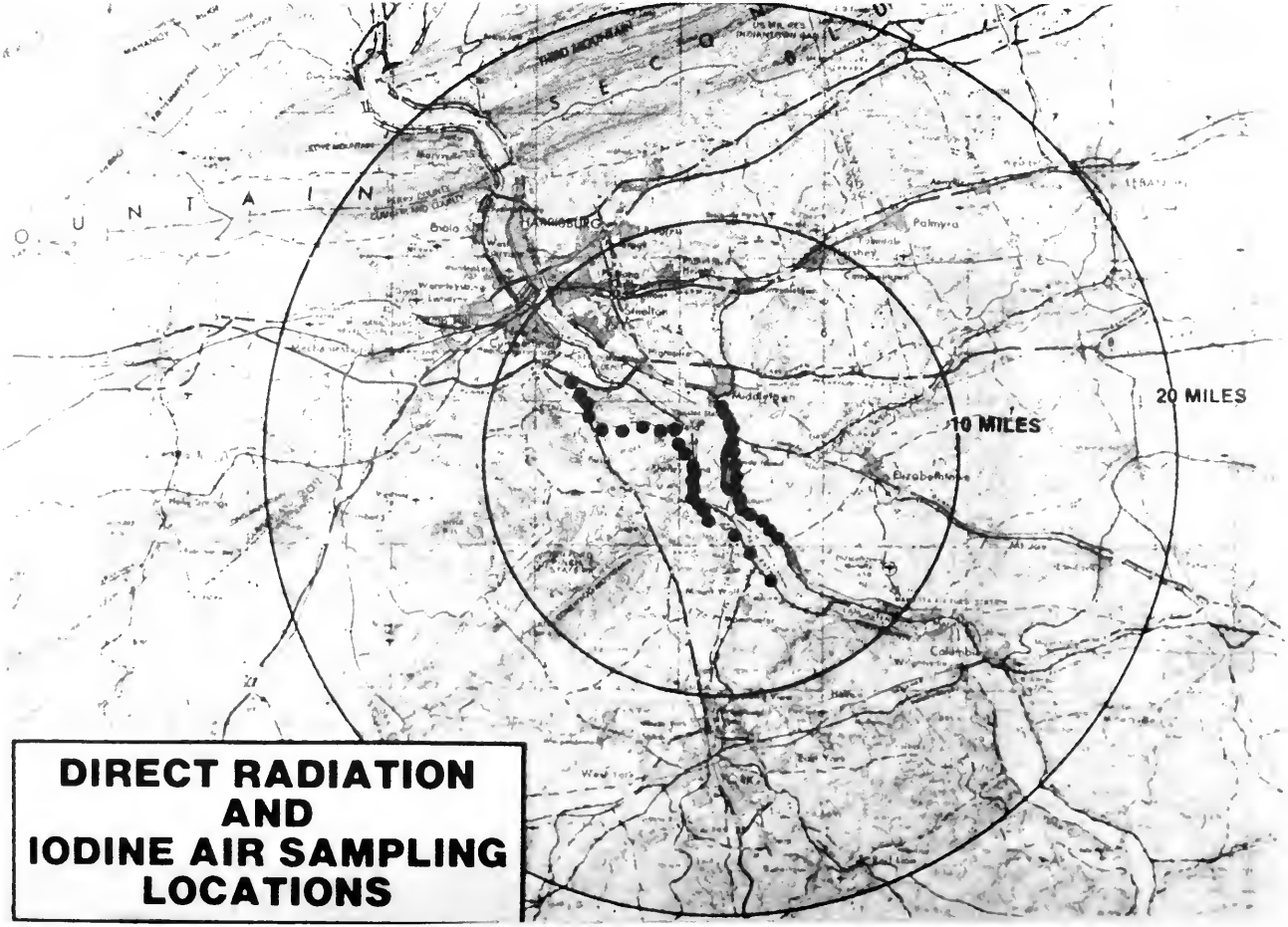


Figure 9: Sampling locations for airborne I-131.

Table 8

AIRBORNE RADIOIODINE

Location	Period	Concentrations
Observation Tower 2.3 mile SSE (Met. Ed)	3/29/79 - 3/31/79	20 pCi/m^3 (2×10^{-11} $\mu Ci/cm^3$)
Observation Tower (Met. Ed)	3/31/79 - 4/3/79	1.4 pCi/m^3 (1.4×10^{-12} $\mu Ci/cm^3$)
Trailer City NRC	4/1/79 - 4/4/79	$<9 \times 10^{-13}$ $\mu Ci/cm^3$
Trailer City NRC	4/5/79	1.6×10^{-12} $\mu Ci/cm^3$

Table 9

CHILD'S THYROID

	Dose (mrem)
First three day period 3/29/79 - 3/31/79 concentration 2.3 mi SSE	2.7
Second three day period 3/31/79 - 4/3/79	0.19
NRC data assume 2 x 10 $^{-12}$ $\mu Ci/cm^3$ for period 4/2/79 - 4/3/79 (some overlap with record three-day period	0.18
	3.1

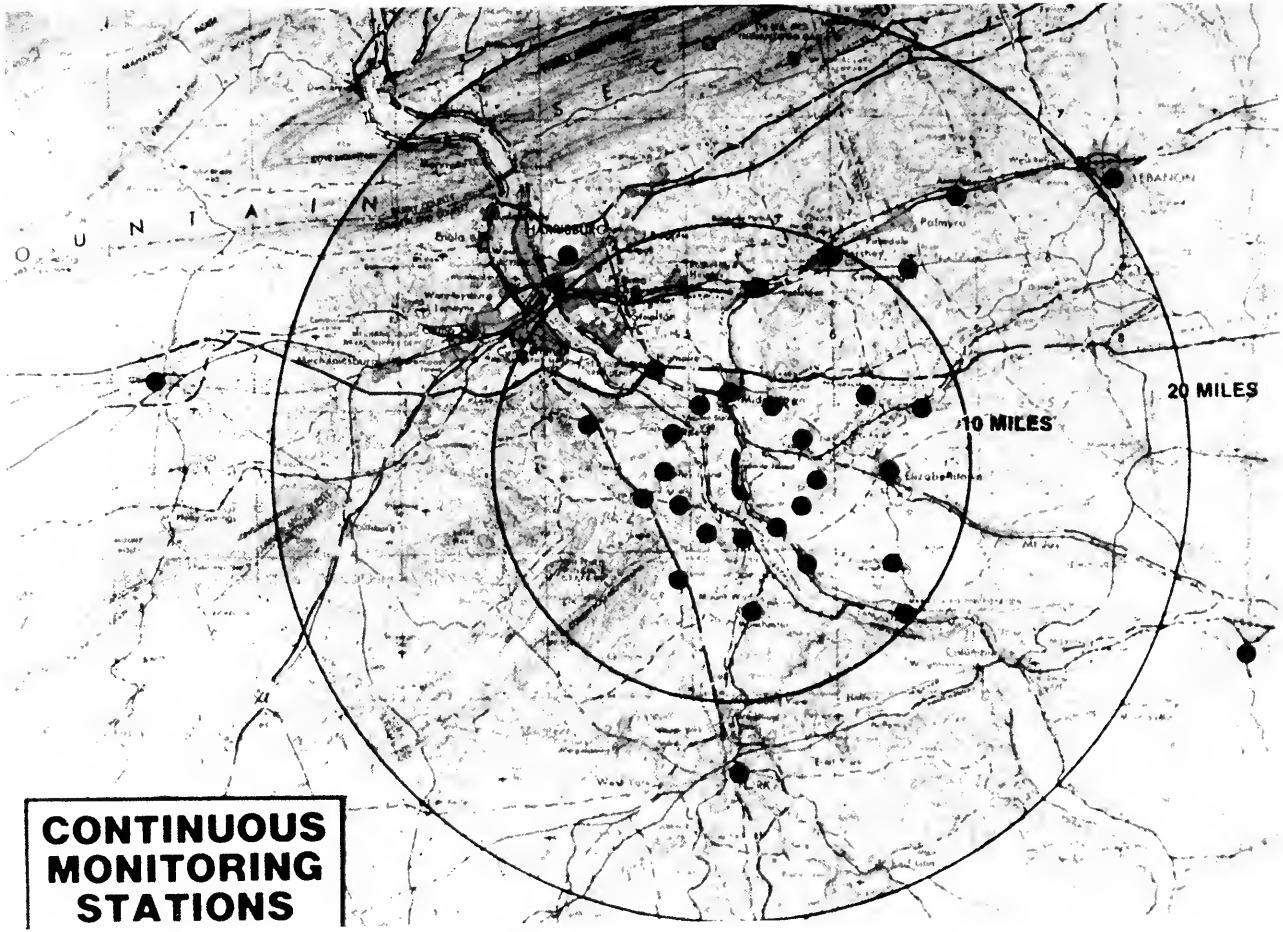


Figure 10: Continuous monitoring locations

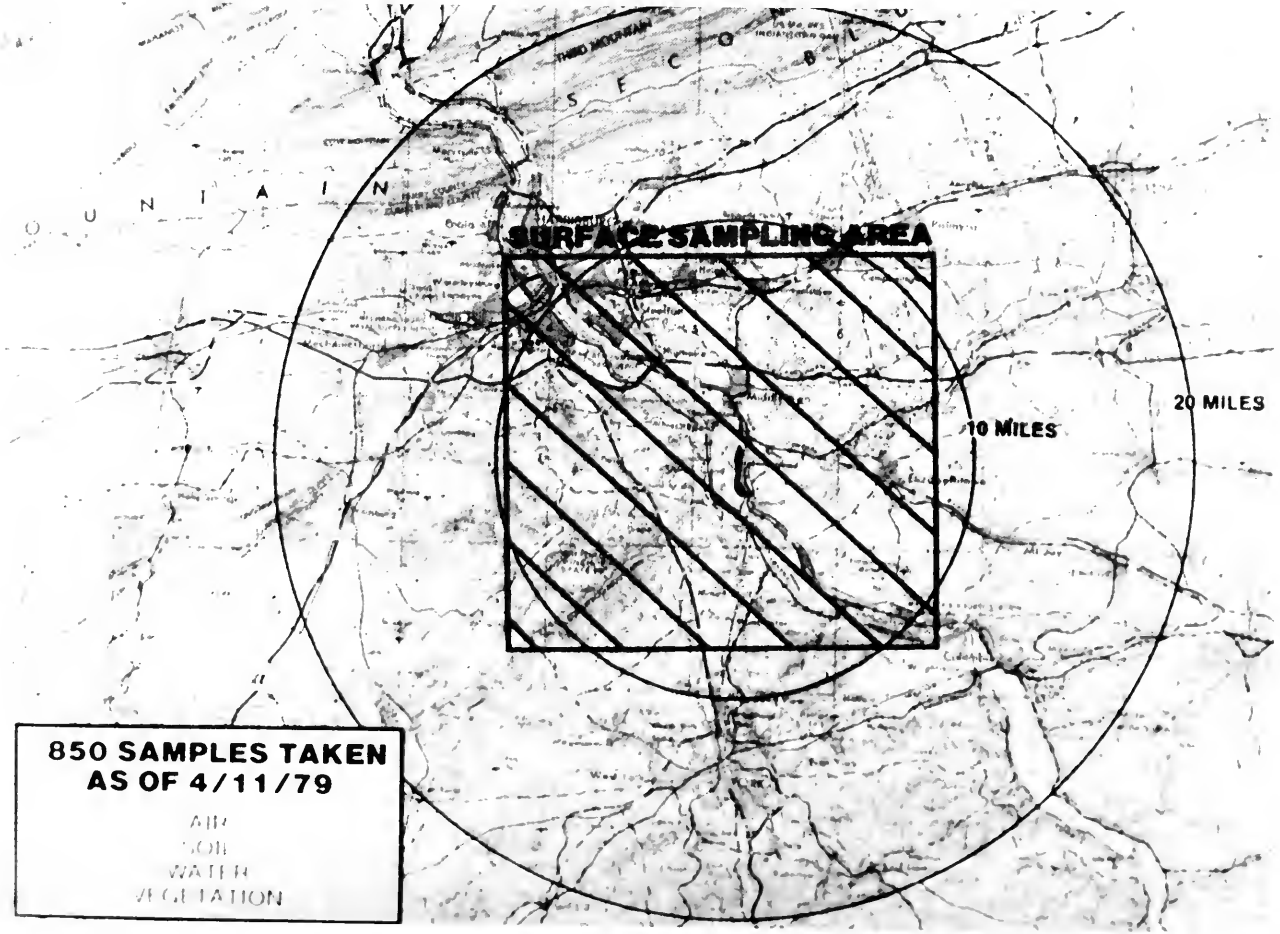


Figure 11: Sampling area for air, soil, water and vegetation

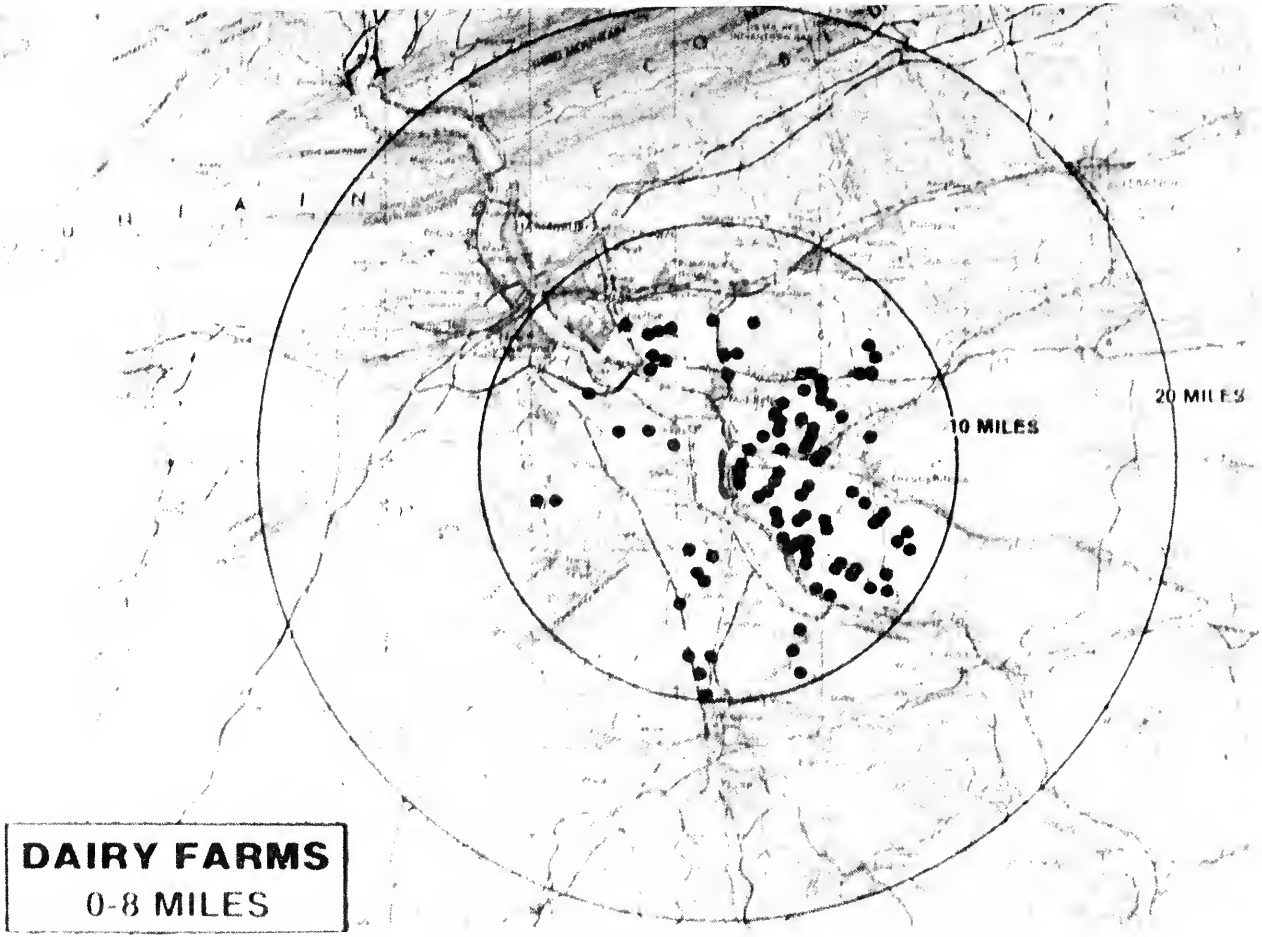


Figure 12: Location of dairy farms within 10 miles of TMI

Table 10

MILK ANALYSES

	Pennsylvania	FDA	EPA	Metropolitan Edison
Number of analyses performed	133	84	4	21
Number of positive results	7	53	2	18
Average value of positive results (pCi/ℓ)	15	19	17	7
Range of positive results PCi/ℓ)	11-20	9-41	10-24	1-41
Average minimum detectable activity (pCi/ℓ)	<20	<10	<10	<1

sensitive detector system inside some very dense shielding in order to block the detection of cosmic radiation and the other external radiation sources to permit the detection of very small amounts of radionuclides that do get into the body. One sees a readout of the pertinent energy spectrum, so one can identify which radionuclides are present.

There was a large whole body counting program provided for the area population in Middletown and 721 people availed themselves of it. Only nine showed anything in the way of radioactivity that differed from the general population and none of the radioactivity was attributable to radio-iodine or fission products. The isotopes found were primarily the Radon family and had to do with the type of housing that the particular individuals lived in. These essentially negative results confirmed the environmental monitoring data.

Also, the Department of Health arranged for urine samples to be analyzed by N.I.H. and no radio-iodine or other radioactive elements were being excreted in 39 people that were studied that way. These results provide biological corroboration of the dosimetry program's results that I have reviewed for you.

What does this mean in terms of early health implications, which is my assignment today? To give you orders of magnitude again, Table 11 presents the classical acute evidences of radiation injury, the acute radiation syndrome as summarized by Dr. George Voelz of Los Alamos Scientific Laboratory. Here you see the doses are not in millirad or millirem, but in rads, which is 1,000 times higher, so that 50 rads would be 50,000 millirads. You can see that the TMI area population exposure was down at a level where none of these acute effects would show up. Indeed, the most sensitive indicators we have for diagnostic purposes for evaluating and detecting acute early radiation effects are listed in Table 12. Again, you can see that the minimum exposures which produce any of these clinically detectable health impairments or changes that can be seen by our most sensitive diagnostic indicators are an order of magnitude or more too high. In other words, the lowest detection limit is about 10 rads (10,000 millirads), and we cannot accurately detect individual biological effects below that, which we think of as a low level of exposure.

For these reasons, early biological response to the estimated radiation exposure of this population would be completely undetectable by clinical diagnostic study. You may say that is just because one is unable to find and measure it; but in my view what is clinically undetectable cannot be considered a health impairment. Thus, this review of the TMI radiation dosimetry data brings us the reassuring conclusion that there was not enough radiation exposure to affect the individuals in the off-site population of the area in terms of early health effects.

Acknowledgements The author wishes to express his appreciation to Lewis Battist, NRC, for making very preliminary information available from the Ad Hoc Population Dose Assessment Group effort, to Joe Deal, DOE, for providing monitoring data and E.G. and G. data displays. Without their prompt assistance, this presentation would not have been feasible. Tables 1 through 10 and Table 12 were derived from the Ad Hoc Group's data, while Figures 2, 5 and 6 through 12 were from E. G. and G. Figure 1 was from the New York Times, Figure 3 from Time magazine, Figure 4 from Metropolitan Edison Co., and Table 11 from Los Alamos Scientific Laboratory Report LA-UR-75-1023.

Table 11

Dose-Effect Relationsnips for Acute Whole Body Exposure:

DOSE-EFFECT RELATIONSHIPS FOLLOWING ACUTE

WHOLE BODY IRRADIATION (X- OR GAMMA)

Whole Body* Dose (rad)	Clinical and Laboratory Findings
5 - 25	Asymptomatic. Conventional blood studies are normal. Chromosome aberrations detectable.
50 - 75	Asymptomatic. Minor depressions of white cells and platelets detectable in a few persons, especially if baseline values established.
75 - 125	Minimal acute doses that produce prodromal symptoms (anorexia, nausea, vomiting, fatigue) in about 10-20% of persons within 2 days. Mild depressions of white cells and platelets in some persons.
125 - 200	Symptomatic course with transient disability and clear hematological changes in a majority of exposed persons. Lymphocyte depression of about 50% within 48 hours.
240 - 340	Serious, disabling illness in most persons with about 50% mortality, if untreated. Lymphocyte depression of about 75+% within 48 hours.
500+	Accelerated version of acute radiation syndrome with gastrointestinal complications within two weeks, bleeding, and death in most exposed persons.
5000+	Fulminating course with cardiovascular, gastro-intestinal and CNS complications resulting in death within 24-72 hours.

* Conversion of rad (midline) dose to radiation measurements in R can be made roughly by multiplying rad times 1.5. For example, 200 rad (midline) is equal to about 300 R (200 x 1.5).

Table 12

RADIATION INJURY EVALUATION TESTS

TEST	FINDING	MINIMUM EXPOSURE
Symptom History	Nausea, Vomiting	~ 100 rads
Physical Exam	Erythema	> 300 rads
	Epilation	> 300 rads
Blood Count	Lymphocytes-<1000/mm^3	~ 100 rads
Sperm Count	< 20 M	~ 15 rads
Cytogenetics	Aberrations	~ 10 rads

Dr. Sternglass: Number one: Why was this meeting organized in such a way that many of us who have been studying low level effects in the last few years, as a matter of fact, decade, were not invited to provide the balance, proper balance, to this presentation? Now that's the first question I'd like to ask. The second question is, oh, would you like to answer that?

Dr. Shrivastava: Yes I would. The questions are to be of the topic the speaker is speaking on, please. It's because we only have a few minutes for questions. They have to be specific and they have to be short. We will not take papers from the floor. So please ask your questions very quickly.

Dr. Sternglass: I thought it was our intention here to get to the bottom of what might have been going on. And I think it is totally unfair and totally not within keeping of a scientific meeting to restrict questions in that manner. Now let me place my question. And I'm doing this under protest, because I asked to be given an opportunity to participate in order to provide the people with the both sides of the question. Alright, now let me go on.

Dr. Shrivastava: Question please.

Dr. Sternglass: Why, for instance, have you in your dose estimates for the population, confined yourself to the TLD reading, after Karl Z. Morgan, the first president of the Health Physics Society and head of the Oakridge National Laboratory, testified in congress at the Kennedy meeting, that the TLD's could not read the beta dose? And if you do take the beta dose into account according to Alan Brodsky's work, who was here in your department of the University of Pittsburgh, and is now with Nuclear Regulatory Commission; according to him, the inhalation doses from iodine would be 37 times as large for the adult and much larger for the fetal and infant thyroid (Page 45). And if one were to consider all the fission products the total doses would be 100 to 200 times greater than those that you have just put on the board. Furthermore, how can you explain that when the tapes were released, which no one had expected to see, that the measurements carried out by the NRC and reported were 1200 millirems per hour in the plume and the same day in the P & O's, which I personally collected, the same maximum dose in the plume was being measured and being reported to the public as 6 to 8 millirems per hour, 200 times less. And those are the problems which are going to have to be answered in the future.

Dr. Wald: I don't know if that was a speech or a question. As far as the beta sensitivity of the detecting equipment, there are calibrations being done at the National Bureau of Standards which haven't been completed at this time. A lot of the

FDA's TLDs were designed for mammography studies and they are responsive to the same energy range that you are referring to. Karl Morgan probably is aware that these are relatively low energy radiations and, therefore, have very little penetration to produce any health impact as far as the inhaled dose is concerned, since the dose is from the Xenon-133 primarily, which I take it you are referring to.

Dr. Sternglass: No, I'm referring to a whole series of gasses, there was no indication that just Xenon-133 came out, there was a whole slue of fission gasses coming out.

Dr. Wald: That is not correct in the assessment that I have. Obviously I am relying on the measurements of a number of agencies.

Dr. Sternglass: Well, the NRC talks about a series of fission gasses. They did not, in their own tapes, refer merely to Xenon-133.

Dr. Wald: I have no access to NRC tapes. I don't think that is scientific data.

Dr. Sternglass: No, it was unofficial data.

Walter Pincus: (Washington Post) In the estimated dose, you gave a total of 86 millirem. You divided it up for the 28th and 29th for 45 millirem, which is the first two days of the incident and those, I guess, are essentially the company TLDs.

Dr. Wald: And the State.

Walter Pincus: Well, 17 and 4.

Dr. Wald: One other thing let me mention. By 4 p.m. of the 28th, the NRC dosimeters were in place. It's only that first 4 a.m. to 4 p.m. that relies on what was already out in the field, on the 28th.

Walter Pincus: Well, NRC told me that they didn't put them in till Saturday evening.

Dr. Wald: Not the TLD dosimeters, but they were making measurements with Geiger Muller counters.

Walter Pincus: Right, but they didn't put the TLDs in till Saturday. Now the second phase you had was the 29th and the 31st and you had the exposure dropping down to 29 millirems but that covers the period of the plume, the largest escapings. So you have less measurement during the period of the largest escape of radiation. Is that correct?

Dr. Wald: Yes, as I pointed out, the initial measurements are based on what was in the field before the incident, because if there

was enough foresight to put dosimeters to monitor an incident, I guess there wouldn't have been an incident.

Walter Pincus: Well, no, the ones that were in the field were covering the previous quarter, they were covering 3 months, is that 45 millirems for 3 months total measurement or is that their estimate of what happened in those 2 days. So that's an estimate essentially.

Dr. Wald: It includes a correction from shelf dosimeters that weren't in the field.

Walter Pincus: But you agree that your own figures show that after the plume was released you had less measurement than you did before the plume was released.

Dr. Wald: No. The initial measurements were with what was there to start with. Not less than what was there.

Walter Pincus: I'm not talking about the measuring device, I'm talking about the millirem measurement. You got to 86 essentially by having 45 millirem the first 2 days. You then had 29 millirem the next two days which would cover the period of the largest release of radiation.

Dr. Wald: Yes.

Walter Pincus: So it went down?

Dr. Wald: The numbers I gave you are the best estimates based on the TLD's information. I can't go on beyond that. Don't attribute the numbers to me.

Walter Pincus: Well, who do we attribute the numbers to.

Dr. Wald: The NRC and the DOE in particular.

Walter Pincus: OK, now if you follow the train of thought, then you pick up very low exposures. If you then go to the person-rem estimate, which I gather are based on those measurements times the number of people....if you just take your first set of figures the people living from 0 to 10 miles, the 28th and 29th you showed 206 person-rems. Is that correct? Because the next set of figures which cover the 29th to the 31st, if they follow your initial ones, should go down. And, in fact, they measure 764 person-rem which is as I measure, 3 times the first ones. So it's just inconsistent.

Dr. Wald: Well, I'll have to review the numbers with you, I don't know how to do it here.

Jerry Rosen: This is not a question; it is a comment on the last speaker's question. During those first 48 hours, presumably, the plume was spreading and more people were getting exposed to lower level, but the population dose as a whole would go up, due to the spread of the plume and the larger population involved. That could explain the rise in the number.

Dr. Shrivastava: That's a good point.

Editor's note: Dr. Brodsky sent me the following response (dated April 30, 1979) to the question on inhalation dose.

As I discussed with you by telephone on Friday, I would like to make the following response to Dr. Sternglass' comment in Pittsburgh on April 25, 1979, that the NRC-reported doses did not correspond to calculations in my paper "Criteria for Acute Exposure to Mixed Fission Product Aerosols" (Health Physics 11, pp 1017-1032, 1965), in which he claims that the "typical mix" would give 30 rem lung dose per curie sec/cubic meter and 10 rem to the thyroid compared to only .28 rem from external irradiation, quoting Table 8. These rem and thyroid doses, as well as other results of Table 8, were calculated under the assumption that a large fraction of radioiodines and other fission products were released from the hypothetical reactor. As I have stated in public on a number of occasions since the Three Mile Island accident, the containment buildings retained a remarkably high proportion of those radionuclides that escaped from the reactor vessel, so Dr. Sternglass is quoting results based on assumptions that are not applicable to the Three Mile Island accident. Evidence from whole-body counting of more than 700 persons shows very definitely that the amount of internal exposure from radioiodine or any other radionuclide has been negligible and could not be even one millionth of the dose calculated in my hypothetical accident. Indeed, the NRC and its predecessor regulatory agency carried out such hypothetical calculations for the very purpose of designing containment to prevent releases of the type that Dr. Sternglass believes occurred but which did not occur.

I hope that my statement will clarify the situation and alleviate concern.

Signed, Allen Brodsky, Sc.D.

GENETIC EFFECTS

Seymour Abrahamson, Ph.D.

My purpose today is to try to make reasonably clear the methods that have been developed to estimate the genetic risk to the offspring of a human population who have received an added increment of radiation. Natually occurring genetic disorders account for a considerable amount of human ill health and suffering. We presently estimate (BEIR III) that some 10.7% of all newborn suffer or will suffer (in their lifetime) from serious diseases of genetic origin.

The kinds of genetic changes that underlie the genetic diseases are of several types, and are deserving of a brief discussion.

Gene mutations represent the largest category of significant genetic alterations. Mutations may result from subtle derangements in the chemical structure of the gene such as substitution of one nucleic acid base for another in the polynucleotide sequence (1000 or more bases) that determines the specific properties encoded for by that gene. Or they may involve the loss/addition of one or more such bases even including the loss of entire sequence and beyond. For the most part, we do not have the same resolving prowess for discriminating these different changes in the higher organisms as we do in viruses, bacteria and other lower organisms. In man (and other animals as well) the mutation may be manifested in different ways, 'dominant recessive' or 'X-linked '. The dominant mutations manifest themselves in offspring when present with a normal gene for the same function contributed by the other parent, while the recessive mutation requires that both parents contribute the same defectively functioning genes to the offspring in order for the expression of deviant appearance. Sex-linked mutations are most frequently expressed in males who by virtue of their inheriting only one X-chromosome must, therefore, demonstrate the presence of X-linked mutant genes. In addition to these simply inherited single gene-type disorders, there is a very large class of disorders that involve complex interactions both among a multiple of genes and in conjunction with environmental factors.

Two kinds of chromosomal changes also contribute to the genetic disease burden. 1) Those that result from chromosome aberrations as a result of breakage and rearrangements of genetic material. 'Translocations' and 'Inversions' are among the major kinds of chromosome rearrangements of this class. Such rearrangements, per se, may result in abnormality, or the rearrangement may subsequently lead to progressive disruption of the normal complement of genetic material as a result of meiotic divisions which reshuffle the genetic material during the formation of the gametes. 2) During these meiotic divisions, the failure of normal separation of homologous pairs of chromosomes from each other will lead to gametes which are seriously imbalanced. That is to say that the gametes (and later on zygotes) will have either one extra or missing chromosome from the complete set required for normal development. Tables 1 - 7 (taken from C. O. Carter's paper) provide examples of the most common genetic disorders of the types mentioned above, their estimated frequencies and body systems influenced.

Table 1

Estimates of birth frequencies of some more common dominant conditions in European derived populations per 1000 live births

Nervous system	Huntington's chorea	0.5
	Neurofibromatosis	0.4
	Myotonic dystrophy	0.2
Intestines	Multiple polyposis coli	0.1
Kidney	Polycystic disease of the kidneys	0.8
Skeleton	Diaphysial aclasis	0.5
Sight	Dominant forms of blindness	0.1
Hearing	Dominant forms of early childhood onset deafness	0.1
	Dominant otosclerosis (adult onset)	3.0
Circulation	Monogenic hypercholesterolaemia	2.0
Teeth	Dentinogenesis imperfecta	0.1
Blood	Congenital spherocytosis	0.2

Tables 1 through 7 are from C. O. Carter, Progress in Genetic Toxicology, 1977

Table 2

Estimates of birth frequencies of some more common dominant conditions in European derived populations per 1000 live births

Nervous system	Huntington's chorea	0.5
	Neurofibromatosis	0.4
	Myotonic dystrophy	0.2
Intestines	Multiple polyposis coli	0.1
Kidney	Polycystic disease of the kidneys	0.8
Skeleton	Diaphysial aclasis	0.5
Sight	Dominant forms of blindness	0.1
Hearing	Dominant forms of early childhood onset deafness	0.1
	Dominant otosclerosis (adult onset)	3.0
Circulation	Monogenic hypercholesterolaemia	2.0
Teeth	Dentinogenesis imperfecta	0.1
Blood	Congenital spherocytosis	0.2

Table 3

FREQUENCIES OF SOME OF THE COMMON LATE ONSET CONDITIONS WITH DOMINANT INHERITANCE

DISORDER	FREQUENCY PER 1000 LIVEBORN
Monogenic hypercholesterolaemia	2.0
Huntington's chorea	0.5
Multiple polyposis coli	0.1
Polycystic kidney disease	0.8
Adult onset dominant otosclerosis	1.0
TOTAL	4.4

Table 4

Estimate of the birth frequency in males of the more common X-linked conditions in European derived population per 1000 live births

Locomotor system	Muscle dystrophy - Duchenne	0.2
Blood clotting	Haemophila A	0.1
Skin	Ichthyosis	0.1
Mental retardation	Non-specific X-linked	0.1

Table 5

Estimates of birth frequencies of some more common recessive conditions in Britain per 1000 live births

Metabolism	Cystic fibrosis	0.5
	Phenylketonuria classical	0.1
Nervous system	Neurogenic muscle atrophies	0.1
Red blood cells	Sickle-cell anemia	0.1
Endocrine glands	Adrenal hyperplasias	0.1
Hearing	Severe congenital deafness	0.2
Sight	Recessive forms of blindness	0.1
Mental retardation severe	Non-specific recessive forms	0.5

Table 6

Births	Anomalies	Births	Anomalies
Male	XYY XXY other	female	X XXX other
34872	29 34 30	20807	2 20 7
	0.27%		0.14%

Table 7

Births	Trisomies	Unbalanced structural	Total unbalanced	Balanced structural
	+D +E +G other			
55679	3 7 63 3	30	106	107
	0.14%	0.05%	0.19%	0.19%

The late Professor Trimble and his colleagues have provided us with some estimates of the impact of genetic disease on the health burden. As shown in Tables 8 - 9, genetically determined infant mortality contributes the major component of such mortality, perhaps as much as 80% and accounts for the largest number of hospital days spent by children up to age 5, relative to all other causes. I think this type of information more dramatically points up the genetic disease role in the social costs of ill health.

I should like to next move on to the subject of radiation genetics in order to acquaint you with some important principles and issues. The shape of the mutation dose response curve is critical for an understanding of risk extrapolation (interpolation) to very low doses, such as background exposure or from the release at Three Mile Island. With very few exceptions, when a mutation dose response curve for acutely delivered X or γ radiation is developed which includes an extensive number of dose points, the shape of the curve often best approximates that of a linear quadratic function, namely, a linear rising curve in the low dose region with a faster rising (dose ^{2}) portion of the curve at increasing doses. The precise points of inflection vary with respect to the species of organism studied and very possibly as a result of the total content of DNA per nucleus. The theoretical and practical significance of these dose response curves is that they indicate that the mutation frequency (gene or chromosomal) in the quadratic region of the curve can be modified by altering the manner in which the dose is delivered, either by dose protraction, dose fractionation or by some similar combination of these elements. This implies that some form of damage-repair is available to the cell when the dose is not delivered in some nearly instantaneous fashion. Moreover, the genetic lesions may require two events to be induced and they are the result of independent ionizing tracks in the quadratic region of the curve (where they are dose rate dependent), while the two lesions are probably the result of single ionization tracts (the region of densely clustered ionizations) in the linear (dose rate independent) portion of the curve.

A second important point is that different radiations (X, α,neutron) are for the same physical dose differentially effective in the production of genetic damage. The relative biological effectiveness (RBE) is a measure of the effectiveness of a radiation source compared with 250 kVp x-rays. It would appear that the ratio of slopes of the two radiations taken from the linear portions of their dose-response curves would constitute the most accurate measure of the RBE. The 'rem' dose referred to in the later sections of this talk and others today represents an adjusted dose with respect to RBE and other modifying factors.

In the next several figures, I shall attempt to reconstruct for you how the various committee reports (BEIR I, BEIR III and others) have attempted to estimate genetic risk from irradiation. In Table 10, we see that a best estimate of the human gene mutation rate is between 0.5×10^{-5} and 0.5×10^{-6} per gene and that the induced mutation rate per gene (mouse germ cells irradiated at low dose rates) averages for both sexes in the range of 0.35 to 0.5×10^{-7}mutations/gene/R. The dose required to double the spontaneous mutation rate, the doubling dose, can be obtained by dividing the spontaneous rate by the induced rate. For the numbers I have chosen, the doubling dose is between 10 and 140 rem; however, the BEIR I committee used a value of

Table 8

INFANT MORTALITY FOR SELECTED KINDS
OF CHILDHOOD HEREDITARY DISORDERS
(DEATHS PER 1,000 AFFECTED)

	TOTAL CASES	MORTALITY	FACTOR INCREASE OVER ALL BIRTHS
ALL LIVEBIRTHS	810,089	25	
DOMINANTS	370	81	x 3.2
RECESSIVES	559	88	x 3.5
CONGENITAL MALFORMATIONS	14,467	118	x 4.7

Table 9

NUMBER OF DAYS HOSPITAL STAY PER 100 AFFECTED CHILDREN WITH CERTAIN KINDS OF CHILDHOOD HEREDITARY DISORDERS

AGE	1	2	3	4	5
ALL LIVEBIRTHS	225	70	40	35	30
DOMINANTS	2500 (x11)	1150 (x16)	500 (x13)	350 (x10)	1200 (x40)
RECESSIVES	3000 (x13)	900 (x13)	450 (x11)	700 (x20)	350 (x12)
CONGENITAL MALFORMATIONS	1300 (x6)	600 (x9)	360 (x9)	280 (x8)	330 (x11)

Table 10

CALCULATION OF THE RELATIVE RISK FOR MONOGENIC DISEASES

1) Spontaneous Human gene mutation rate $0.5 \times 10^{-5} - 0.5 \times 10^{-6}$ (A)

2) Induced gene mutation rate

per roentgen from mouse spermatogonia	0.7×10^{-7}
from mouse oocytes	$\underline{0 - 0.3 \times 10^{-7}}$
Average	$0.35 - 0.5 \times 10^{-7}$ (B)

3) Doubling dose $\frac{0.5 \times 10^{-5} - 0.5 \times 10^{-6}\ (A)}{0.35 \times 10^{-7} - 0.5 \times 10^{-7}(B)} = 10 - 140$ Roentgen

This is the dose of radiation required to double the number of mutations that occur naturally.

4) The relative mutation risk per roentgen $= \frac{1}{10} - \frac{1}{140} = .1$

20 - 200 rem, while the UNSCEAR committee chose a single value of 100 rem for their calculations and BEIR III derived values ranging between 50 and 250 rem. The inverse of the doubling dose is called the relative mutation risk per rem and is used to estimate the contribution to the disease burden from an increment of exposure. In Table 11, we describe the assumptions required to determine what the effects of 1 rem will be in terms of the next generation or if there is a continuous additional exposure of one rem to each and every subsequent generation until a new equilibrium is attained.

For dominant-gene-based diseases, these assumptions suggest that 14 - 200 additional cases will be observed in the next generation per million liveborn per rem of parental exposure. Note that these cases are in addition to the 10,000 naturally occurring cases in that same population. Similar calculations are carried out in Table 12 to provide an estimate of the number of new cases of complexly inherited diseases either in the next generation or at equilibrium. Additional assumptions are required for this calculation. Perhaps the most sensitive assumption is the mutational component for these diseases. For dominant diseases, the mutational component is 1.0 which essentially means that each new mutation is expressed as a disease, whereas, a mutational component of 0.05 implies that the chance of expression is 1/20 that of a simple dominant. Thus the rate of increase is much slower.

The present, and as yet unpublished, BEIR III report also provides a different method ("direct") of assessing first generation dominant diseases. The procedure essentially determines an observed frequency of induced skeletal abnormalities in the male offspring of mice for a given dose of irradiation and estimates what the whole body disease frequency will be under a given set of assumptions that would be applicable to man. These estimates range from 5 - 65 additional cases per rem of parental exposure per million liveborn. This is about one-half the values estimated by them by the doubling dose method. Both the direct and indirect approaches, however, are dependent upon a large number of assumptions requiring further verification.

Examination of Table 13 provides the current incidence of genetic disease for all genetic categories previously discussed and the estimates of some different groups published or in preparation. The number of anticipated genetic diseases clearly is influenced by the specific assumptions employed in deriving doubling dose values (such as spontaneous mutation rates and induced male and female mutation rates), mutational components, equilibrium time, the shape of dose response curve, etc. I have not attempted here to outline the procedures used to calculate the estimated number of chromosome determined diseases but it is based on observations of human male exposure and a variety of assumptions concerned with the transmissibility and viability of such chromosome abnormalities.

The larger value of chromosome diseases associated with the Ford-Mitre report is based on a study in mouse oocytes which has not been substantiated in subsequent studies and, therefore, may well over-estimate the contribution from this class of disease.

Having taken you through the risk-estimate lottery, my charge for this presentation was to estimate the total number of genetic effects to be

Table 11

AN EXAMPLE OF THE APPLICATION OF THE RELATIVE MUTATION RISK

ASSUME 1) A POPULATION WERE EXPOSED TO 1 ROENTGEN FOR MANY GENERATIONS

2) THE CURRENT INCIDENCE OF SINGLE GENE DETERMINED DOMINANT DISEASES IS 10,000 PER 10^6 PEOPLE

3) THE EQUILIBRIUM TIME FOR DOMINANT DISEASES IS 5 GENERATIONS

A) THEN 1 R WILL INCREASE THE INCIDENCE OF DOMINANT DISEASES BY 1/10 - 1/140. AT EQUILIBRIUM THERE WILL BE OBSERVED BETWEEN 10,070 AND 11,00 DISEASES/10^6.

B) IN THE FIRST GENERATION AFTER EXPOSURE THERE WOULD BE 14-200 NEW DOMINANT DISEASE CASES/10^6 PER ROENTGEN OF EXPOSURE.

Table 12

CALCULATION OF THE RELATIVE MUTATION RISK FOR IRREGULARLY INHERITED DISEASES

1. Assume same Relative Mutation Risk as obtained for monogenic diseases namely 0.1 - 0.007 per roentgen

2. Assume the mutational component lies between 0.05 and 0.5

3. Assume the equilibrium time is 10 generations

4. The current incidence of these diseases $\tilde{=}$90,000 per 10^6 liveborn

A. Then at equilibrium expect 90,000 (0.007 - 0.1) (0.05 - 0.5) = 32 - 4500 cases induced per roentgen

B. At first generation expect between 3-450 cases/R/10^6

Table 13

ESTIMATED FIRST GENERATION GENETIC EFFECTS OF ONE REM OF RADIATION PER 10^6 LIVEBORN

Type of Damage	Current* Incidence	BEIR I (20-200)**	First Generation Ford-Mitre (5-50)	Wash 1400 (100)	A (10-140)	B	C***
Autosomal Dominant	10,000	10-100	40-400	20	14-200	5-65	10
X-linked recessive	400	0-3	1-15	1	1-6		1
Irregularly inherited	90,000	2-150	9-900	5-50	3-450		2-25
Chromosomal							
A. Unbalanced rearrangements	500	6	20-40	6	20-40	0-10	14
B. Numberical	4,000	1	1-25	1	1-25		25
Geometric mean		70	300	50	170	20	60

* Values of each study adjusted to same current incidence figures.

** Doubling dose ranges.

*** Study C used a doubling dose of 225 for dominants, 70 R for other monogenic diseases and a mutational component of 0.02-0.2 for irregularly inherited tracts.

predicted from the Three Mile Island exposure. Since this talk was presented, we have estimates that place the average population exposure between 1 to 2 millirem for the 2 million people. On the basis of these figures, one can estimate that no more than 0.6 radiation induced cases can be expected in the next one-million births which are estimated to occur over the next 30 years. The number could be considerably lower. Recall that the same number of births will include over 100,000 cases of naturally occurring defects. It would be tragic indeed if enormous expenditures were devoted to tracking this next generation for putative induced effects when, if properly directed, such expenditures can have enormously greater health benefits.

RADIATION EFFECTS ON THE DEVELOPING EMBRYO

Robert Brent, M.D.

I have been asked to discuss with you the effects of radiation on the developing embryo. This information comes from several areas. It comes from past exposures to human populations of pregnant women, those from the early 30's who were exposed to radiation because they were pregnant and concomitant carcinoma of the cervix or the uterus. Populations of women who were exposed in Hiroshima-Nagasaki, individual case reports and then, of course, epidemiological studies involving the women exposed to diagnostic radiation.

In the 40's and 50's, pelvimetry was a diagnostic technique used to determine the size of the fetus and pelvic outlet. For those of you who are not aware of it, it is a technique that is used much less because of the availability of other techniques such as sonography. And then there is the vast amount of information developed during the last 30 years dealing with the effects of radiation on the non-human mammalian embryo.

We have difficulty in many areas of transposing animal data to the human population. Thalidomide, a drug which produced malformations in the human population, was not teratogenic in the rat. Such exceptions between human and animal effects indicate that there are marked differences in the effects of chemical teratogens among species. Yet, of all the teratogens that we've studied, there is better correlation among species with radiation than with any other teratogen. You don't have to be concerned with the maternal metabolism of a drug. Does the rat metabolize a particular drug differently than the human? This is not a problem with radiation. Secondly, you don't have to worry or be concerned about the difference in placental transport because the mouse placenta or the rat placenta is different from the human placenta. Thirdly, radiation is uniformly distributed in the tissue; there are no receptor sites to be concerned about. Radiation uniformly causes an exposure in all the tissue and, so from the theoretical basis, there is much greater likelihood that animal data within certain limitation can be used to evaluate the effects of radiation in the human better than any other known environmental teratogen.

Now, with regards to the effects of high levels of radiation to the embryo, we can observe a radiation syndrome. By high levels of radiation, I mean radiation exposure a person would get from radiation therapy for cancer of her abdomen, or that women in Nagasaki-Hiroshima received within 1500 meters of the bomb. These women received 50 to 250 rads of radiation. There were consistent findings in a percentage of the offspring that we call the radiation syndrome. This is a triad of effects; lethality if the dose is high enough, intrauterine growth retardation and gross congenital malformations. The congenital malformations are very obvious, those that you don't have to be a physician to recognize.

The first aspect of this triad; namely the production of congenital malformations has quantitative limitations. In the TMI episode, a tremendous amount of misinformation was generated to the public, much of it causing unnecessary anxiety. You get this feeling that everybody who is pregnant is

equally sensitive to radiation at all stages of pregnancy and it doesn't matter what the dose is. What I'm going to demonstrate is that the embryo is really constantly changing with regard to its sensitivity and response to radiation. As the embryo goes from a single cell organism to a very complicated organism at term, there are marked changes in its responses to both external and internal radiation.

Let's look at the so-called malforming effects of radiation. What you find on the abscissa in Figure 1 is weeks of human gestation. On the ordinate, you find the incidence of malformation, in other words, the proportion of offspring in an exposed population that you would expect to be malformed. If you use 100 rads, which is within the therapeutic dose of radiation and the kind of radiation you might get from an atomic bomb exposure, you find that there is a very short period of mammalian gestation (called the period of early organogenesis during which the three germ layers are forming all the organs and tissues), during which the embryo is extremely sensitive to the malforming effects of radiation. This period would be equivalent to between the 12th or 14th day to around the 30th day of human gestation.

There is a period from menstruation to the time of conception, when a woman is not pregnant, which you wouldn't be concerned about. The next period is from the time of conception to her first missed mentrual period. During this period, (the first 14 days of gestation) , there is a very interesting phenomenon called the 'all or none response'. There the embryo cannot be malformed, regardless of exposure, but it is very sensitive to the killing effects of radiation. So, during this period, 100 rads can eliminate 65-70% of mammalian embryos. But the ones that would survive, interestingly enough, would be completely normal.

The last part of the first trimester, and the latter two trimesters, can be affected by radiation. But we don't observe serious, grotesque, gross malformations. We can observe minor malformations following exposure in the latter part of the first trimester. In the last two trimesters, we observe cell deletions or cell depletions.

The embryo intrinsically determines the number of cells it should have as an adult. Somehow, when we start out with an egg and a sperm, we know that when we become an adult we're going to have so many hundreds of billions of cells and we stop. But there are times in our development where, if we interfere with cellular growth, the embryo cannot recoup. With high dosages, you can decrease certain cell structures so that they will be permanently small. These cell deletions can result in tissue hypoplesia, small organs or a reduced number of cells. So in reality, there is no time in gestation where the embryo can't be affected by a dose of 50-100 rads of radiation.

Now, let's look at some of these phenomena. First of all during the all or none phenomenon, 150 rems (or 150 thousand millirems) of radiation on the first day of gestation will produce 60 to 70% embryonic deaths (Figure 2). The surviving embryos will be normal in structure and, interestingly, will grow normally. They will reach normal weight and development as an adult. Yet, during this period of gestation, the embryo is extremely sensitive to the killing effect. We've done some low level studies with 30 thousand millirems,

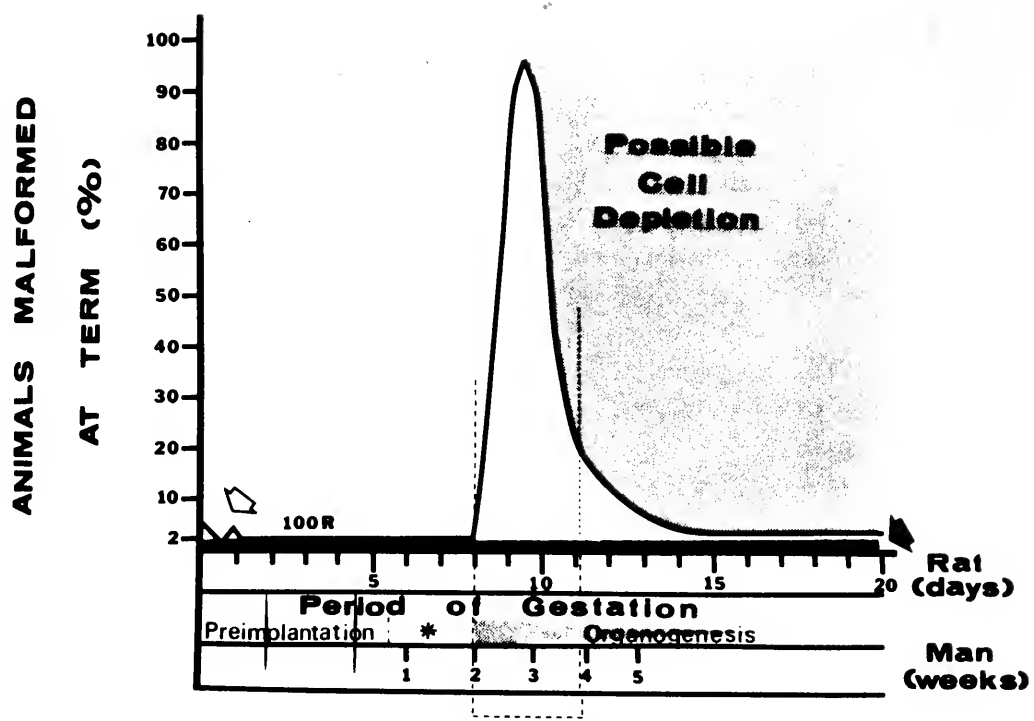


Figure 1: Incidence of malformation with 100 rads exposure vs. period of gestation

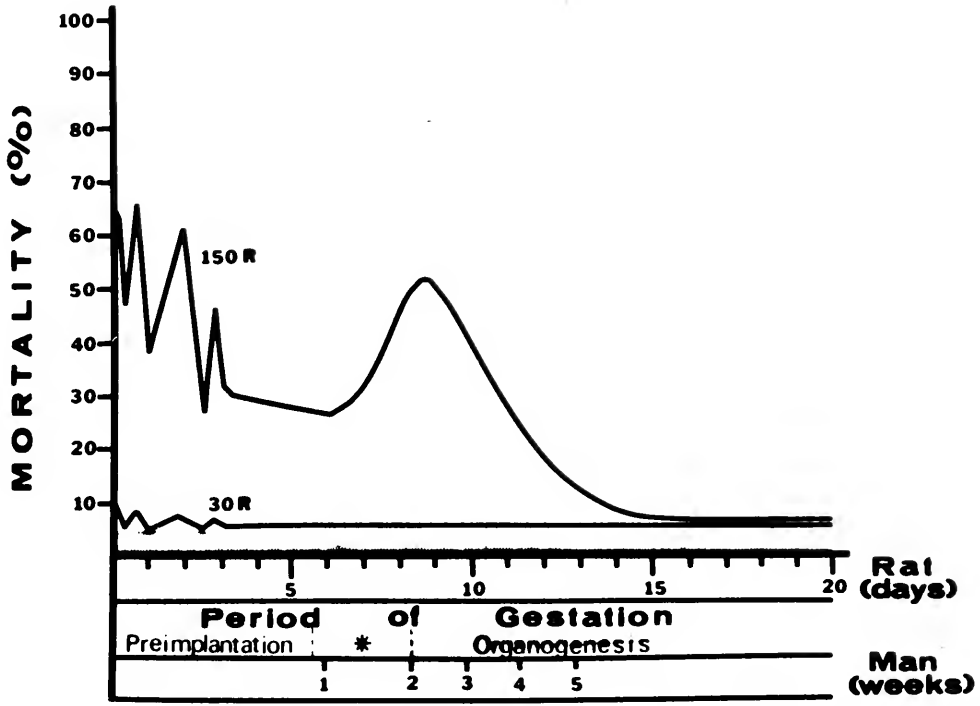


Figure 2: Mortality from exposure to 30 R or 150 R vs. period of gestation

20 thousand and 10 thousand millirems and we find (Table 1) that we can increase the mortality with increasing dose during this period of development. A 10 thousand millirem dose can increase the resorption rate to almost double the control level of resorption in a rat. However, when we got down to 5 thousand millirem, we found that there was no increase in mortality. Thus, there seems to be a threshold effect somewhere around 5 thousand millirem with regard to lethality.

Now, what does this mean? Well, it just so happens that the mammalian embryo is extremely sensitive, very vulnerable to killing effects. For instance, in our laboratory, we find that exposure to alcohol, which just reaches the level of 150 milligrams per cent, can produce 18% resorption and that aspirin of about 200 milligrams per kilogram produces a 14 to 15% resorption rate. So nature has built in this marked embryo sensitivity early in development such if things aren't right, the embryo dies. If the embryo is not killed somehow, it's able to get through that period and produce a normal offspring and that is why we refer to this as an all or none phenomenon. I want to indicate that this phenomenon is not specific for radiation. It is operative for many noxious environmental agents.

With regard to gross malformations, if the embryo absorbs 100 rads of radiation, you can observe central nervous system malformation effects in 41% and malformation of eyes in 90% of the cases. But at 100 rads, we're talking about large doses of radiation.

Now, tissue hypoplasia is something that the laboratories interested in embryonic development are just beginning to study. Dr. Samual Hicks studied brain hypoplasia when he was at the New England Deaconess Hospital, back in the 50's. You can produce small brains with these large doses of radiation late in gestation. Do you call this congenital malformation or tissue hypoplasia? It's a matter of semantics, but it is an effect. Similarly, you can produce small testicles very late in gestation near term in a rat with 150 rads (Table 2). It's a dose related phenomenon and, surprisingly, the animals' testes may be only 1/5 the size of a normal male, yet they have reproductive potential. Your first impression would be that the animals with small brains were deficient and yet these animals were not able to be distinguished from the controls. Nor were the animals with very small testes able to be discerned from the controls. But this is a serious biological effect with potentially important consequences. Both these effects are dose related and as you lower the exposure to 25 to 30 thousand millirems, the effect disappears. You don't see small brains; and you don't see small testicles.

Dr. Dekaban, a pediatric neurologist at the National Institute of Health, accumulated 20 odd cases of patients who were exposed to high doses of radiation in utero. These pregnant women had cancer of the reproductive organs and were receiving thousands of rads, millions of millirads, of radiation. With irradiation in the period of organogenesis, in that first trimester, he consistently observed mental retardation. If any malformations were present, small head size or eye malformations were consistent findings in the child. For those irradiated in the 2nd and 3rd trimesters, he reported no abnormalties (but there was no way for him to pick up tissue hypoplasia or cell depletions). This clinical data certainly fits in with the data in the animals

Table 1

EFFECT OF X-IRRADIATION EXPOSURE ON THE FIRST DAY OF RAT GESTATION

EXPOSURE	# PREGNANCIES	RESORBTION RATE	TERM FETAL WEIGHT	MALFORMATION RATE
0 R	41	4.7%	5.01G	.2%
10 R	40	11.9%	4.90G	1.6%
20 R	43	13.7%	4.93G	.4%
30 R	43	18.3%	5.02G	.5%

Table 2

FFECT OF LEVEL OF IRRADIATION AT 20TH DAY OF ESTATION ON SEXUAL DEVELOPMENT IN MALE RATS
Murphree

evel of adiation	Weaning wt.(gm.)	Mature wt.(gm.)	Testes wt.(gm.) (68 days)
0	39	283	3.1
12.5	37	277	3.0
25	39	282	3.2
50	31	255	2.3
100	34	256	.7
150	38	260	.6

I want to point out the inconsistency in animal data and human data. We observed in Hiroshima-Nagasaki mental retardation, microcephaly without mental retardation, growth retardation and other associated malformations. We never observed radiation induced malformation that was not associated with undersize, mental retardation, microcephaly or eye malformation. In other words, if you see a child that has no arms and weighs 7 lbs. 2 oz. (which is a normal weight) and is mentally normal whose mother received a chest x-ray during pregnancy, you can tell from experimental data that the child's malformation is from other causes and not from radiation. There has never been a malformation in any other organ that wasn't associated with undersize and one of the central nervous system malformations. In the human, why do we not see all those serious malformations observed in the rat? The reason is because there is no exposure to the human population on an experimental basis. All exposures are at random throughout the nine months of pregnancy and the period of organogenesis makes up a very small percentage of human pregnancy. Therefore, any inadvertent exposure will expose the sensitive embryos in a very low incidence. Furthermore, in an inadvertent exposure like an atomic bomb, those embryos that are sensitive are going to resorb. In women who are getting cancer treatments, the dose will be way above the LD/50 dose. If the mother is receiving radiation during organogenesis, then most of the embryos will resorb. Thus, in humans, we see primarily central nervous effects because the brain's sensitivity persists into the latter part of the 1st and 2nd trimester. So, there is a reasonable explanation for the predominance of CNS effects in the human.

Now, the one other effect that has been talked about is a protracted effect of radiation. What happens when you administer a malforming dose (150 rads or 100 rads) and you spread it out over a period of time? In our own laboratory experiments, we administered high dose radiation (150 rads) at four dose rates, 100, 34, 1.2 and 0.5 rad/min which would mean we had to expose the animals in the lowest dose rate group for a period of 5 hours. Certain malformations occurring at a relatively high incidence in the high dose rate group disappeared at the low dose (Table 3). So the embryo, in spite of its great sensitivity, also demonstrates the same sophisticated repair mechanism as other mammalian cells. Now, that doesn't mean these embryos were not damaged at 150 rads, but only that the effect was markedly reduced as you extend the dose delivery from minutes to hours.

Figure 3 is the work of a neuropathologist at the University of Iowa by the name of Brizee. He studied the effects of cell depletion phenomenon in the brain. He found that if he gave a dose of 150 rads to the brain on the 12th day in the rat, he could markedly decrease the thickness of the cerebral cortex. If he took that same 150 rads of radiation (150 thousand millirad) and fractionated it into 9 dosages over a period of 12 hours, he found that the thickness of the cortex was the same as the controls, again indicating that the embryo, although it is sensitive, has a sophisticated repair mechanism.

I would like to call your attention to two large studies (Stadler and Gowen and Brown and Coppenger, University of Texas and University of Iowa) that were done in the 50's and 60's. They had a Cobalt-60 facility whereby they could lower this radiation source into the floor so that the men or women could

Table 3

% MALFORMATIONS
DOSE RATE R PER MINUTE

	OR	.5	1.2	34	100
ANENCEPHALY	0	0	3.1	13.7	30.3
MICROCEPHALY	0	0	20.3	41.1	9.1
HYDROCEPHALY	.5	29.5	14.1	26.0	24.2
MICROSTOMIA	0	0	7.8	16.4	31.8
EVISCERATION	0	0	4.7	6.8	16.7
RENAL AGENESIS	0	0	2.6	5.5	21.2
CLEFT PALATE	0	11.5	17.8	37.5	51.5

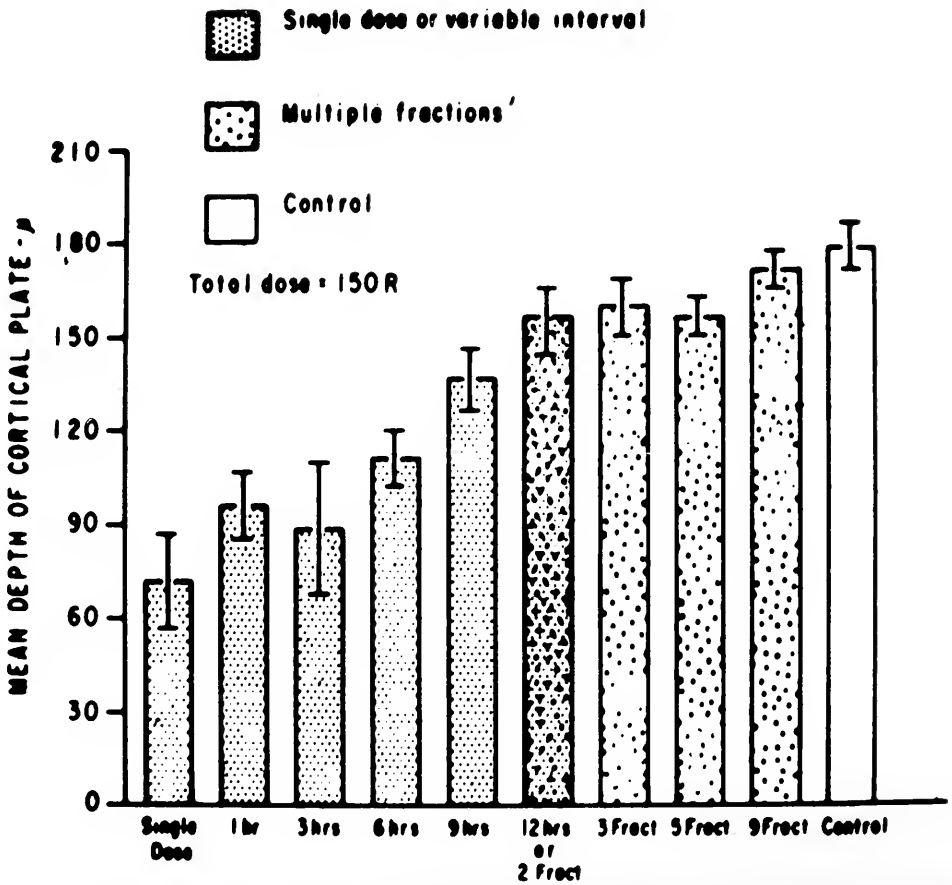


Figure 3: Mean depth of cortical plate in single-dose, control, variable-interval and multiple fraction series.

come in and feed the animals for a period of a few hours a day. Then they would return the source and the animals could receive anywhere from 1 rad per day up to 50 rads per day. They studied these populations of rodents for not one generation, but 10 and 11 generations of continuous radiation from conception to conception. In otherwords, a continuous exposure was given to the animals who were never out of the radiation field except for the few hours each day. At the level of 2 thousand millirem per day of continuous radiation for 11 generations and 2.2 thousand millirem per day for 10 generations, there was no biological effect that they could see: no change in reproductive capacity, no change in the size of the embryo, no change in incidence of malformation, no change in longevity, no change in behavior. We sometimes forget these long term studies. Scientists frequently think the only thing that is ever done is during their active tenure and they ignore literature from the past that may be important. There are other studies, Liane Russel from Oakridge did a study where she gave 12,400 millirem per day to one generation from conception to birth and wasn't able to find any effects.

The next part of the radiation teratology syndrome is the effect on growth. 150 rads, 150 thousand millirads, can produce growth retardation over a longer period of gestation than that in which you can produce malformations. In other words, the sensitivity to the growth retarding effects of radiation begins before the sensitivity to the malforming effects of radiations and it persists all the way to term. If you give a large enough dose, not only to a term embryo or a term human being, but even to a 2 year old child, you can stunt growth. We found, in studying growth, that when we got down below 30 rads we could no longer produce growth retardation. Thus, 30 rads seems to be the level below which we cannot produce small embryos. Dr. Rugh, at Columbia University, did an interesting study. He gave 100 rads on every day of gestation as a single experiment and followed the animals to adulthood. Then he measured their weight. What he found was that 100 rads before organogenesis resulted in animals that weighed the same as controls. The embryos that were most susceptible to permanent growth retardation were not the animals irradiated during early organogenesis, but the animals irradiated during the early fetal stages.

The one other aspect that we should talk about is leukemia induction following fetal radiation exposure. Some investigators have reported an increased sensitivity of the embryo to the leukemogenic effect of radiation. Now let's look at the data Dr. Alice Stewart, a physician in England who used the Oxford data dealing with malignancy, came up with an interesting report (1956-1958). She reported that exposure of the population of women who received pelvimetry late in gestation had a 50% increase in probability that their child would have leukemia. Now, you must understand that leukemia is not a common disease. It occurs 3 per 100 thousand population in caucasian American children and, therefore, what she is saying is that in the population that had pelvimetry, the incidence would be 4.5 per 100 thousand. If you ask the population on the street what it means to have a 100% increase in the leukemia following radiation exposure to pregnant women?, I will guarantee you that 30% of the population will think it means that everybody is going to have leukemia. It sounds sort of stupid but that is what people think when you say there will be 100% increase in leukemia.

I don't know what is the cause of cancer. And I don't think anybody else does. We do not know the multiplicity of factors involved and any piece of information that can be helpful in understanding etiology is important. Dr. Stewart's report that there is a statistical association between leukemia and radiation exposure in utero is therefore important but we don't know if this association is due to selection or whether it is directly due to radiation exposure.

Now, there are very good epidemiologists; one by the name of McMahon who corroborated Dr. Stewart's findings. He found in a large series the same 50% increase of leukemia. Then, 11 other studies were reported. Four of them couldn't find the association, seven of them could. The interesting thing that developed is a perplexing biological contradiction. Graham, who is a radiation biologist at the University of Chicago, reported another control group. He included women who received radiation before they became pregnant as sort of a super control. He found an increase of leukemia in that population. As a biologist, information on the animal population or the human population has to make sense. When that finding was reported, it didn't make sense. We have no evidence that you can produce, with preconception genetic changes, the same disease in the population at the same incidence as with an exposure to a hazard during conception. The mechanisms are all together different and it makes you think maybe there is a selection factor in such studies that we haven't uncovered.

Now, the story gets more interesting. Graham not only found leukemia increased following preconception radiation but after post-conception radiation as well. The data from Hiroshima-Nagasaki included 17 thousand patients radiated and nonradiated first generation offspring without an increase in malignancy. Finally, Kato and Wood evaluated 1000 control and exposed babies in utero and looked at the incidence of malignancy. They found no increase in leukemia even though these children had received anywhere from 10 to 200 rads, which is 10 to 200 times the exposure that Dr. Stewart observed in her study.

So here we have information that is very confusing and cannot document, at this time, if there is an etiological relationship or a selection phenomenon. Now, what are some of the other things that are confusing? Every population that has been studied with an environmental hazard exposure to pregnant women for leukemia induction has been positive. Smoking women's children have a higher incidence of leukemia. Babies that are heavy have a higher incidence of leukemia. Bross, in the New England Journal, shows a history of allergy in the family produces a higher risk for leukemia in the offspring than does radiation exposure. So, all I can tell you is, from a scientific standpoint, this is extremely confusing data. Now, how do you use it?

From a radiation protection vantage point, you use the worst, most pessimistic standpoint. You assume the worst risk and you don't expose pregnant women to any radiation. That is what the NCRP has done, as well as the ICRP. But when it comes to saying to a population that has been exposed, what does this mean, it's very difficult to accurately predict the increased risk. If you look at the data, Alice Stewart's for example, it means that there will be a very slight increase in incidence of leukemia. Certainly, the Harrisburg pregnant population is so small and the dose is so low that you couldn't

calculate one new leukemia due to this radiation exposure. I don't think it's fair for me to say that there is no radiation effect at these low levels because we do not know that.

Let's summarize. What does all this mean with regard to what I've just said? Table 4 summarizes some of the risks for leukemia as compiled by Robert Miller of the NCI. Look at some risks for leukemia. Which population has the highest risk of leukemia? It's a very good question for medical students because you would never guess the answer. It is an identical twin whose sibling has leukemia. The risk, according to the NCI (they have 70 children like that) is 1 in 5 to 1 in 3. If you have an identical twin who has leukemia, you have about a 1 in 5 chance of getting leukemia. That's the highest risk population we have for malignancy.

The U.S. population has 1 leukemia in 3000 over 10 years; Dr. Stewart's data with 50% increase in risk from radiation would support 1 leukemia in 2000 over 10 years. But look and compare this to some of the other risks. If you have a brother or sister with leukemia, according to the NCI, you have a 1 in 720 risk of having leukemia. This is 3 times greater than a prenatal radiation maximum possible effect. So some of the risks that have been put into perspective are helpful in order to understand what we're talking about in the rarity of some of these problems.

The minimum dose for recognizable gross malformations is somewhere around 20 to 25 thousand millirems. The minimum lethal dose on the first day of gestation is around 10 thousand millirems and then it goes up rapidly in later stages.

The LD50, the dose when you would expect half the mammalian embryos to die, is lowest on the first day. The minimum dose for nonrecuperative growth retardation in the adult as I mentioned it to you is about 25 to 30 thousand millirems.

Now, there is a problem in that there are some questions that we can answer. I don't know if we will ever be able to accurately answer them. You ask me, what is the lowest incidence of arsenic in food that will cause some of these effects? or What is the minimum dose for the induction of genetic carcinogenic and minimum cell depletion phenomenon in the embryo? I don't know the answer. All we can do to answer such questions, is project known maximum effects at higher doses linearily into the low dose ranges. This is the most pessimistic viewpoint because it overestimates the risk in an attempt to protect the population.

As I mentioned to you before, we get about three calls a week from pregnant women who have been exposed inadvertantly to diagnostic radiation. It's much different on a one to one basis when you are talking to a woman on the phone who doesn't want an abortion or didn't want to have the baby. It's a complicated medical care issue and there is no way to sort that out at a conference like this. How do you deal with a woman who has been exposed? All I can say is, it isn't only related to the radiation exposure.

If you are talking about a 200 millirem exposure, the calculations I did

Table 4

GROUPS AT EXCEPTIONALLY HIGH RISK OF LEUKEMIA

Group	Approximate Risk	Time Interval
Identical twins of children with leukemia	1 in 5	Weeks or months
Radiation-treated polycythemia vera	1 in 6	10-15 years
Bloom's syndrome	1 in 8	<30 years of age
Hiroshima survivors who were within 1000 meters of the hypocenter	1 in 60	12 years
Down's syndrome	1 in 95	<10 years of age
Radiation-treated patients with ankylosing spondylitis	1 in 270	15 years
Sibs of leukemic children	1 in 720	10 years
U.S. caucasion children <age 15	1 in 2880	10 years

Miller, Cancer Res. '67

would be that you don't expect to get malformations with this low dose. You don't expect to get growth retardation. You don't expect to get increased embryonic death. Some of these are very difficult to measure, such as cell depletion effects and the incidence of leukemia. Even with maximum risk calculations, there would be less than one expected case of leukemia in the offspring of mothers who were pregnant within a 50 mile radius of Three Mile Island. The genetic effects would also be so low that they will not be able to be perceived over the next 30 generations. This is obvious since the population in Japan, which recieved significantly higher exposures, have not manifested any increase in genetic disease.

In summary, the known effects of radiation on the mammalian embryo and human embryo in particular, have been discussed and it should be obvious that there is a great deal of information known about the effects of radiation on the embryo. Not only is the embryo very sensitive, but it also has excellent repair and recuperative powers. This information is frequently ignored by scientists and physicians when they become involved in predicting the effects of embryonic radiation. The exposure at Three Mile Island, of approximately 1-2 millirem per person and including a population of 2 million people, will result in no measurable biological effects and absolutely no increase in the incidence of congenital malformations, growth retardation or embryonic death in the exposed embryos. The greatest impact of the TMI accident is the fear and anxiety present in the population following the accident.

Dr. Wald: A comment - I want to congratulate Dr. Brent in his well documented presentation and his careful attribution of the work to the various sources that he used and it reminded me that I made an oversight and I should hasten, for the record, to attribute the research with the helicopter and the plume following to the Department of Energy and the analysis in terms of man rem, in particular, to Andy Hall of Brookhaven National Laboratory and, now I can face Dr. Bond, the Associate Director of Brookhaven National Laboratory again.

Dr. Concannon: The question is directed to Dr. Brent. Assuming that the data from England is true, a 50% increase in leukemia means risk going from 3 per 100 thousand to 4 per 100 thousand. We know these patients, during an AP and lateral pelvimetry examination, may be getting doses in the range of 20 rads, which is 20 thousand millirads. The reported 50% increase in leukemia, therefore, corresponds to this dose. Now, if you would extrapolate that effect back to, say, 200 millirem dose on the Sigmoid curve in the Primer prepared by Dr. Shrivastava, it would appear to me that any increase of leukemia would come down to zero.

Dr. Brent: The risk is around 1 in 10^{-6} per person. It is one in a million and that is a pretty low risk. It is very hard for me to use the term zero probability for anything and I, therefore, say that there would be less than one case of leukemia on a statistical basis on the TMI population of pregnant women. Less than one case could be 1 tenth of a case, or 1/100th of a case, but that is all I can say.

Dr. Sternglass: Dr. Brent, are you aware of the fact that in Dr. Stewart's 1970 paper, she found a dose response relationship between the number of x-rays given and the risk of leukemia. There was roughly a coubling of risk at about 3 to 4 x-rays typically at 2 to 300 millirem per x-ray or about 1200 millirem for a full term baby, and in the first trimester, 15 times less. In other words, only 80 millirems are needed in the first trimester to double the admittedly small risk of 1 in 2000.

I think perhaps I'd like you also to address a question as to whether or not you are aware of the Diamond study at Johns Hopkins published in the Journal of Epidemiology in May 1973, which was a prospective study that involved many thousand, I believe about 10 thousand individuals, which also confirmed that there is a risk associated with a single 2,3,4,5 diagnostic x-rays in terms of various conditions that express themselves in early death before age 10, including symptoms of the central nervous system.

Dr. Brent: Well, Dr. Sternglass, all that you said is not true, but I'll try to - - - -

Dr. Sternglass: What do you mean, it's not true? Tell me what is not true.

Dr. Brent: What central nervous system? What do you mean, related to the central nervous system?

Dr. Sternglass: In the Diamond-Lillianfeld study, which I advise or suggest that you might want to read.

Dr. Brent: I have read the study very carefully.

Dr. Sternglass: OK, in that case, I'll just remind you that aside from finding a significant increase in leukemia among the white population, I'm now addressing myself to the white population, there are problems with the black population data. With the white population data, they found a significant increase in leukemia rates and also a significant increase in death from what they define or categorize as central nervous system diseases and infectious diseases before age 10.

Dr. Brent: First of all, I noticed that you say that there were problems in the black population. I would consider lack of problems because they didn't have any leukemia. I guess it depends on what you are interested in.

Dr. Sternglass: There is a question as to the nature of the dose response relationship.

Dr. Brent: But you see, when you get a population where you do a prospective study and out of that population you get a black population that does not fit the data and you get a white population that supports your hypothesis, to me, that means that there are problems in trying to interpret. Does this mean again that there was a selection problem? For instance, Dr. Lillianfeld, who was the head of that study, Dr. Diamond was his associate and student at the time; they never analyzed for smoking in the population. Why should we assume that there is only one environmental hazard and one etiology for everything.

Dr. Sternglass: No, nobody assumes that. Obviously, everybody is subjected to all the other environmental agents. Just like the uranium miners, when they smoke, they have 100 times the increase in lung cancer than if they don't smoke, it's only 10 times, so there is no question that whether a woman smokes or takes drugs, it has a very clear synergistic effect.

Dr. Shrivastava: Dr. Sternglass, we could have this discu-sion at the end of the afternoon session.

Dr. Sternglass: Fine. I'm still waiting for the answer to Dr. Stewart's findings that it only takes 80 millirems in the first trimester.

Dr. Brent: Well, let me just answer it now. Do you realize the difficulty it is, retrospectively, to go back and get a history. First of all, do you know where he got the history, from the mother. Secondly, to assume exposure on the basis of the number of films, is extremely unreliable. And all I pointed out is that there are controversies and conflicting data that need to be resolved. And that Stewart's data should be used to protect the population, but it cannot be used to tell people that they are going to get diseases which they may not and probably will not get in the incident that you are saying they are going to get. I can't see any reason to go around not looking at all the information and telling people the worse exaggerated possibility of an exposure when you don't have all the information. I would think that, as a scientist, the thing that you have to say, is we need more data, we need more understanding, we've got to get more information.

Dr. Sternglass: We don't need more Three Mile Islands.

Dr. Brent: Terrific

Dr. Shrivastava: Thank you very much, Dr. Brent, for a very informative talk. Don't misunderstand us, we do want your questions. It's not that we want to stop questions here, but for the sake of time, we have separated a time for questions at the end, in the panel session. So, please, reserve your questions for that time, if you are unable to ask at this time.

THE EFFECTS ON POPULATIONS OF EXPOSURE TO LOW LEVELS OF IONIZING RADIATION

Jacob I. Fabrikant, M.D., Ph.D.

My assignment this morning is to try to give some sort of general background of the implications the 1979 Report of the Committee[1] on the Biological Effects of Ionizing Radiation, National Academy of Sciences-National Research Council, (The BEIR Report) may have on societal decision-making in the regulation of activities concerned with the health effects of low-level man-made radiation (Table 1). I shall try to discuss how certain of the areas addressed by the 1979 BEIR Committee Report attempt to deal with the scientific basis for establishing appropriate radiation protection guides, and how such a Report may not necessarily serve as a review and evaluation of existing scientific knowledge concerning radiation exposure to human populations. Whatever I may consider important in these discussions, I speak only as an individual, and in no way do I speak for the BEIR Committee whose present deliberations are soon to become available. It would be difficult for me not to be somewhat biased and directed in favor of the substance of the BEIR Reports (1-3), since as an individual, I have been sufficiently close to the ongoing scientific deliberations of agreement and disagreement as they developed over the past 9 years.

I think the best thing for me to do is to describe very briefly some of the characteristics of certain aspects of the past and present BEIR Reports (1-3) which may apply to societal decision-making as regards present and future nuclear energy needs and medical care services wherever possible, and to speculate with some educated guessing what we might expect in future deliberations of such expert committees. We need consider only those problems about which most information is now available, only one-third of a century since the birth of the atomic age following the bombings of Hiroshima and Nagasaki, to provide some understanding of those epidemiological and experimental studies likely to be of significance to critical societal factors which must ultimately be considered by all of us, and what relation these studies might have to the affairs of mice and man. Since decisions are to be made involving them, public acceptance must be gained on the basis of providing society with the services that it requires, or that it considers it requires, in the areas of nuclear energy needs and medical care, but with minimum, and wherever possible, negligible risks to its health and its environment.

At the same time, I want to raise a number of questions relating to the need and the wisdom of inclusion of numerical risk estimates in unofficial and official documents, since such documents and such numbers are available to all, to be used and quoted in and out of context. Further, I shall address the appropriate use of such risk estimates for assessment of risk-benefit relationships in the areas of medical radiation exposure and nuclear energy production. And lastly, I would like briefly to conjecture with you in the importance of keeping in proper perspective those pragmatic responsibilities

[1]Committee on the Biological Effects of Ionizing Radiations, National Academy of Sciences - National Research Council, Washington, D.C.

Table 1

The 1979 BEIR Report

1. Societal Decision-Making
2. Nuclear Energy Needs and Medical Care Services
3. Epidemiological and Experimental Studies
4. Public Acceptance
5. Concept of Risks to Health
6. Risk Estimates, Risk/Cost-Benefit
7. Comparison of Risks

of an informed society in the comparison and assessment of all its activities in which there are both acceptable and unacceptable risks, to try to get you to stand up and argue with me and with members of this symposium, or preferably argue with others in this room.

Why Do We Have Advisory Committees on Radiation?

Responsible public awareness of the possible health effects of ionizing radiations from nuclear weapons and weapons testing, from medical and industrial radiation exposure, and from the production of nuclear energy has called for expert advice and guidance in the matter. Advisory committees on radiation of national and international composition have for many years met and served faithfully and effectively to report on three important matters of societal concern: (1) to place into perspective the extent of harm to the health of man and his descendants to be expected in the present and in the future from those societal activities involving ionizing radiation; (2) to develop quantitative indices of harm based on dose-effect relationships; such indices could then be used with prudent caution to introduce concepts of the regulation of population doses on the basis of somatic and genetic risks; and (3) to identify the magnitude and extent of radiation activities which could cause harm, to assess their relative significance, and to provide a framework for recommendations on how to reduce unnecessary radiation exposure to human populations. To a greater or lesser extent, each advisory committee on radiation--such as the UNSCEAR[2], the ICRP[3], the NCRP[4], and the BEIR--deal with these matters, but the reports of these various bodies are expected to differ because of the charge, the scope, and the composition of the Committee, and public attitudes existing at the time of the deliberations of that committee, and at the time of the writing of that particular report. The main difference of the BEIR Report is not so much from new data or new interpretations of existing data, but rather from a philosophical approach and appraisal of existing and future radiation protection resulting from an atmosphere of constantly changing societal conditions and public attitudes.

What is the BEIR Report?

The BEIR Report of the National Academy of Sciences - National Research Council Committee on the Biological Effects of Ionizing Radiation is the record of deliberations of an expert scientific advisory committee (the BEIR Committee) and deals with the scientific basis of the health effects in human populations exposed to low levels of ionizing radiation. The Report broadly encompasses two areas: (1) it reviews the current scientific knowledge--laboratory experiments and epidemiological surveys---concerning radiation exposure of human populations and the long-term health effects of low level ionizing radiation;

[2] United Nations Scientific Committee on the Effects of Atomic Radiation, New York.
[3] International Commission Radiological Protection, Sutton, Surrey, England.
[4] National Council of Radiation Protection and Measurements, Washington, DC

(2) it evaluates and analyzes these long-term health effects---both somatic and genetic effects---in relation to the risks from exposure to low level ionizing radiation. The BEIR Committee is an advisory committee of the National Academy of Sciences - National Research Council. It presently consists of 22 scientific members, selected for their special scientific expertise in areas of biology, biophysics, biostatistics, epidemiology, genetics, medicine, physics, public health, and the radiological sciences. The Report of this advisory committee has, in the past, become an important reference text as a scientific basis for the development of appropriate and suitable radiation protection standards.

How Will the 1979 BEIR Report be of Value?

The BEIR Reports of 1972 (2) and 1977 (3), the Report of the 1955 BEAR Committee[5] (4,5), the parent Committee, and the forthcoming 1979 BEIR-III Report (1) all differ from one or more of the other Committee Reports of the UNSCEAR (6,9), the ICRP (10,13), the NCRP (14,15) and of other national councils and committees (16,17), in five important ways as follows. First, the BEIR Report is not intended to be an encyclopedic reference text, but rather a usable document. A usable document is soon frayed, dog-eared, underlined, and marginated. Thus, the conclusions, recommendations, and appendices are purposefully presented in a straightforward way so that the Report will be useful to those responsible for decision-making concerning regulatory programs involving radiation in the United States. There is no intent, that I can perceive in the BEIR Reports, to make the task any easier or to set the direction for those decision-makers who must take into account the considerations of science and technology and the relevant sociological and economic matters in the development of such regulatory programs. The BEIR Committee has seriously deliberated these issues, and has responsibly addressed them to a greater or lesser extent.

Second, the experimental data and epidemiological surveys are carefully reviewed and assessed for their value in estimating numerical risk coefficients for the health hazards to human populations exposed to low levels of ionizing radiation. Such devices require scientific judgment and assumptions based on the available data only, and has led to disagreement not only outside the committee room, but among committee members, as well. But such disagreement centers not on the scientific facts or the epidemiological data, but rather on the assumptions and interpretations of the available facts and data. Therefore, the BEIR Report uses a particularly valuable format for decision-making, viz., the numerical risk estimates derived are presented logically after the evaluation of the scientific facts and the epidemiological data, and the scientific assumptions on which they are based.

Third, the BEIR Report does not set radiation protection standards. However, it suggests that those that do should always consider societal needs at that time, so that standards are established on levels of radiation exposure which are not necessarily absolutely safe, but rather those which are considered as appropriately safe for the existing circumstances at the time to fill society's needs.

[5]Committee on the Biological Effects of Atomic Radiation, National Academy of Sciences - National Research Council, Washington, D.C.

Fourth, medical and dental radiation exposure is considered of appropriate concern to the health of the public. In view of the enormous growth of medical and dental radiological health care delivered in the United States, the BEIR Committee recommends that medical and dental radiation exposure can and should be reduced to a large extent without impairing the medical or dental benefits to be derived by the individual and to society (1-3).

Fifth, no other advisory committee on radiation has so consistently recommended the need to assess the benefits from radiation to be derived in relation to the risks from radiation to be incurred (1-3). However difficult, tedious and pedestrian this task may be, the BEIR Committee recognized that in any society with limited resources, risk assessment alone could prove to be an academic exercise without some form of benefit assessment to which it can relate. Such benefit-risk, and subsequently cost-effectiveness assessments are essential for societal decision-making for establishing appropriate radiation protection standards. Decisions can and must be made on the value and cost of any technological or other societal effort to reduce the risk by reducing the level of radiation exposure. This would include societal choices centered on alternative methods involving nonradiation activities available through a comparison of the costs to human health and to the environment (2).

What are the Health Effects of Low Levels of Ionizing Radiation?

My remarks will be restricted primarily to those long-term health effects in humans following exposure to x-rays and to gamma rays from radioactive sources, since these are the ionizing radiations most often encountered in medicine and in nuclear industries. Briefly, low-level ionizing radiations can affect the cells and tissues of the body in three important ways. First, if the damage occurs in one or a few cells, such as those of the blood-forming tissues, the irradiated cell can occasionally transform into a cancer cell, and after a period of time there is an increased risk of cancer developing in the exposed individual. This health effect is called carcinogenesis. Second, if the fetus is exposed during pregnancy, injury can occur to the developing cells and tissues, leading to developmental abnormalities in the newborn. This health effect is called teratogenesis. Third, if the injury is in the reproductive cell of the testis or ovary, the hereditary structure of the cell can be altered, and the injury can be expressed in the descendants of the exposed individual. The health effect is called mutagenesis or a genetic effect.

There are a number of other possible biological effects of ionizing radiations, such as cataracts of the lens of the eye, or impairment of fertility, but these three important health effects-carcinogenic, teratogenic and genetic-stand out because; (a) a considerable amount of scientific information is known from epidemiological studies of exposed human populations and from laboratory animal experiments; and (b) we believe that any exposure to radiation at low levels of dose carries some risk fo such deleterious effects. Furthermore, as the dose of radiation increases above very low levels, the risk of these deleterious effects increases in the exposed human populations. It is these latter observations that have been central to public concern about the possible health effects of low-level ionizing radiation, and the task of determining standards for protection for the health of exposed populations. Reports of

expert advisory committees are in close agreement on the broad and substantive issues of such health effects.

Based on careful statistical analyses of epidemiological surveys of exposed human populations, in conjuction with extensive research in laboratory animals on (a) dose-response relationships of carcinogenic, teratogenic and genetic effects, and on (b) mechanisms of cell and tissue injury, a number of important conclusions on the health effects of ionizing radiation has emerged.

1. In regard to radiation-induced cancer, the solid cancers arising in the various organs and tissues, such as the female breast and the thyroid gland, rather than leukemia, are the principal late effects in individuals exposed to radiation. The different organs and tissues vary greatly in their relative susceptibility to radiation-induced cancer. The most frequently occurring radiation-induced cancers in man include primarily in decreasing order of susceptibility, the female breast, the thyroid gland, especially in young children and females, the blood-forming organs (causing leukemia), the lung, certain organs of the gastrointestinal tract, and the bones. There are influences, however, of age at the time of irradiation, of sex, and of the radiation factors and types affecting the cancer risk.

2. The effects on growth and development of the embryo and fetus are related to the stage at which exposure occurs. It would appear that a threshold level of radiation dose may exist below which gross effects will not be observed. However, these levels would vary greatly depending on the particular abnormality.

3. The paucity of human data from exposed populations has made it necessary to estimate genetic risks based mainly on laboratory mouse experiments. Our knowledge of fundamental mechanisms of radiation injury at the genetic level permits greater assurance for extrapolation from laboratory experiments to man. Mutagenic effects are related linearly to radiation dose. With new information of the broad spectrum and incidence of serious genetically-related medical disease in man, such as mental retardation, diabetes, the risk of radiation-induced mutations affecting future generations takes on a new and special meaning.

However, there is still very much we do not know about the potential health hazards of low-level ionizing radiation.

1. We do not know what the health effects are at dose rates as low as a few hundred millirem per year. It is probable that if health effects do occur, they will be masked by environmental or other factors that produce similar effects.

2. The epidemiological data on exposed human populations is highly uncertain as regards the forms of the dose-response relationships for radiation-induced cancer, and this is especially the case for low dose levels. Therefore, it has been necessary to estimate human cancer risk at low doses primarily from observations at relatively high doses. To do this, the linear no-threshold hypothesis has been frequently used, recognizing the lack of our scientific understanding of fundamental mechanisms of radiation-induced cancer in man.

In considering the many forms of the dose-response relationships applied to epidemiological data, the linear model has emerged as the simplest and the most conservative, but not necessarily the universally correct form. However, it is not known whether the cancer incidence observed at high dose levels applies also at low levels.

3. As yet, we have no reliable method of estimating the repair of injured cells and tissues of the body exposed to very low doses and dose rates. And, further, we cannot identify those persons who may be particularly susceptible to radiation injury.

4. From the epidemiological surveys of irradiated populations exposed in the past, we have only limited information of the precise radiation doses absorbed by the tissues and organs, and we do not know the complete cancer incidence in each population, since new cases of cancer continue to appear with the passing of time. Thus, any estimation of risks to health based on such limited dose-response information must be incomplete.

5. Finally, we do not know the role of competing environmental and other host factors - biological, chemical or physical factors - existing at the time of exposure, or following exposure, which may affect and influence the carcinogenic, teratogenic, or genetic effects of low-level ionizing radiation.

Should We Determine Radiation Risk Estimates?

Radiation is firmly-established as a technological activity of modern man; there is no easy way of assessing its worth in medicine, in industry, and especially in energy, and in war and in our peace efforts. But its potential or real benefits do not necessarily outweigh the potential or real risks to human health and to the environment in every instance. What is needed is a method for comparison of these risks and benefits for societal approbation and guidance (1-3). It is logical that to a large extent such guidance and regulation of population doses should be based on the quantitative estimation of risk (1). And here we have a quantitative approach. This concept was introduced by the original 1955 BEAR Committee (5,6), and at that time, the basis of genetic risks was used. But, with the emergence of a large body of scientifically convincing epidemiological data on radiation-induced cancer in exposed human populations, the use of numerical risk estimates, particularly in official documents, begs the question of how safe is 'appropriately safe' for those societal activities in which radiation exposure however small, is nevertheless unavoidable? Thus, it is not surprising that including numerical estimates of serious risks to health in official documents will always prove to be a controversial issue. This arises out of the most perplexing problem of all, and about which we know so little, that of the dose-response relationships for radiation-induced human cancer at low levels of dose (18-20). Here, there is a very large literature, but very little quantitative information on human exposure to radiation with which to work in order to make broad and fundamental societal decisions.

A general hypothesis for estimating the excess cancer risk in irradiated human populations, based on theoretical considerations, extensive experimental animal studies and epidemiological surveys, suggests that a complex dose-

response relationship exists between radiation dose and cancer incidence (18-21). The most widely accepted model (Figure 1), based on the available information and consistent with both knowledge and theory, takes the complex linear-quadratic form $I(D) = (\alpha_0 + \alpha_1 D + \alpha_2 D^2) \exp(-\beta_1 D - \beta_2 D^2)$, where I is the cancer incidence in the irradiated population at dose D in rad, and α_0, α_1, α_2, β_1 and β_2 are non-negative constants. The multicomponent curve contains an initial upward-curving linear and quadratic functions of dose which represent the process of cancer induction, i.e.,carcinogenesis. This is modified by an exponential function of dose which represents the competing effect of cell killing at high doses. The dose-response function illustrated in Figure 1 encompasses all these parameters and is necessarily complex, but certain of the parameters can be theoretically determined. α_0, the control or natural incidence of cancer in the population, is the ordinate intercept at 0 dose of the dose response curve. α_1 is the initial slope at 0 dose, defining the linear component in the low dose range. α_2 is the curvature near 0 dose at the upward-curving quadratic function of dose. β_1 and β_2 are the slopes defining the cell killing function, that is, the downward-curving function in the region of high dose (21).

Review of a large number of the available dose-incidence curves for carcinogenesis in irradiated populations has demonstrated that for different radiation-induced cancers, whether in man or in animals, the extent of variations in the shapes of the curves does not permit determination of any of these values with precesion, or of assuming their values, or of assuming any fixed relationship between two or more of these parameters. In the case of the available epidemiological data on irradiated populations, this general dose-response mathematical form cannot be universally applied. It has become necessary to simplify the model by reducing the number of parameters or by eliminating those parameters which will have the least effect on the form of the curve in the dose range at low levels of radiation. Such simpler models with increasing complexity are illustrated in Figure 2, e.g., linear, quadratic, linear-quadratic, and finally, the linear-quadratic form with an exponential modifier due to the effects of cell killing similar to the general form in Figure 1.

There has been much concern among radiation scientists centering on one particular form of radiation-dose cancer-incidence relationship, generally a linear, no threshold dose-response relationship, that is, where the effect observed is linearly related to dose (Figure 2) (18-20). There is no reason to assume that the linear form, or any form of dose-response relationship, is the inflexibly correct, or the appropriate function either for cells in tissue culture, or for animals in cages, or for man in his society, to warrant universal application in determining public health policy on radiation protection standards. The lack of our understanding of the fundamental mechanisms of radiation-induced cancer in man, and the recognition that the dose-response information from human data is highly uncertain, particularly at low levels of dose, does not relieve decision-makers of the responsibility for determining public health policy based on radiation protection standards. What has emerged from the committee rooms is that estimates of risk, particularly at low doses, must depend more on what is assumed about the shape of the mathematical form of the dose-response function than on the available epidemiological data. In considering the many mathematical functions of increasing complexity, the linear form has emerged by default as the simplest, but not necessarily the

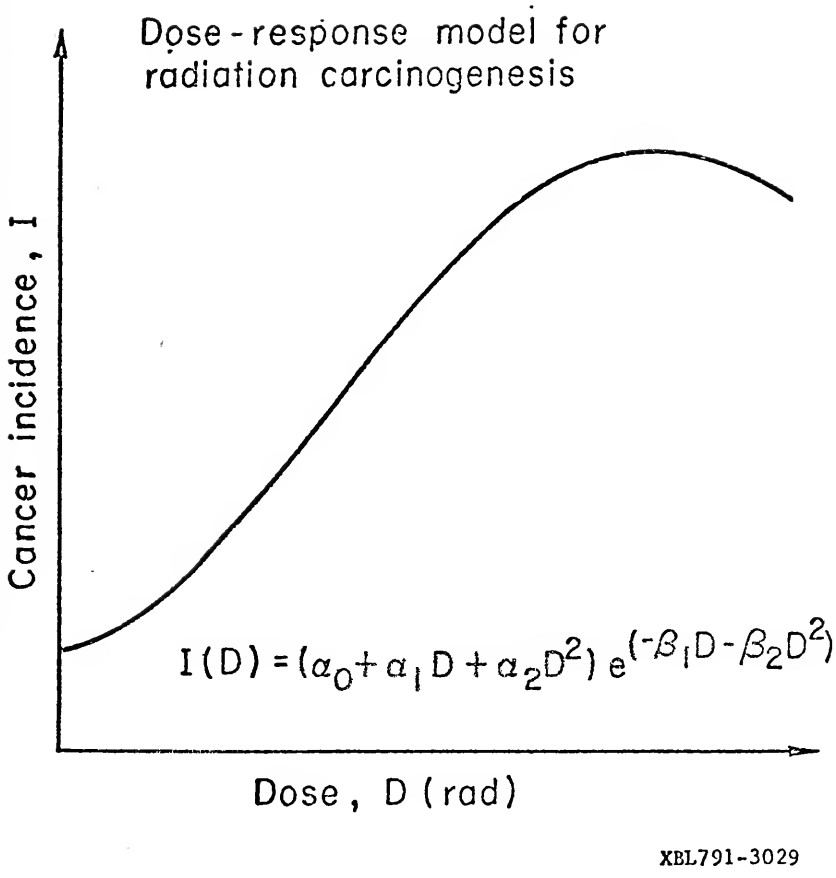


Figure 1. Dose-response model for radiation carcinogenesis.

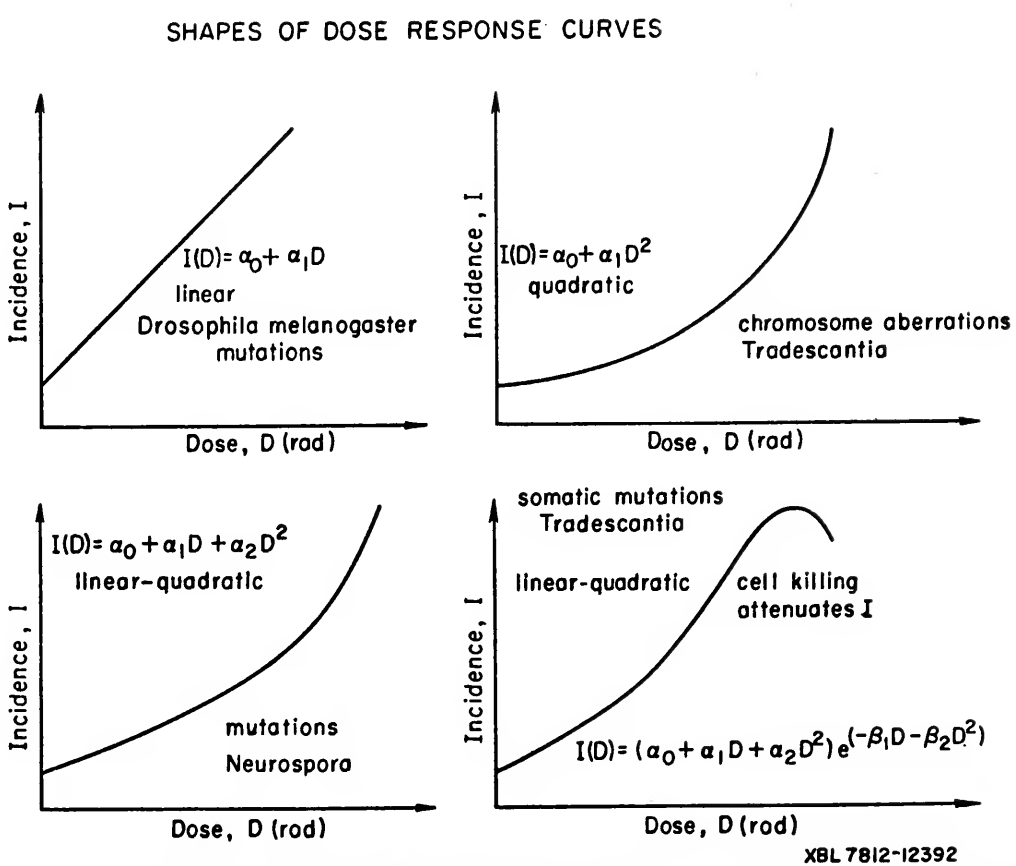


Figure 2. Shapes of dose-response curves.

correct form. We are aware of experimental and theoretical considerations which suggest that various and different mathematical forms of dose-response relationships may exist for different radiation-induced cancers in exposed human populations, indeed for different somatic and genetic mutations (18-21). It is therefore essential that very precise explanations and qualifications of the assumptions and procedures involved in determining such risk estimates are provided, and this has been done explicitly in the BEIR Committee Report containing the estimates of risk. Thus, given all the limitations, it appears that radiation risk estimates for cancer induction by radiation based on linearity are not necessarily spurious, but are estimates only--based solely on what is known. For low LET radiations, such as x-rays and gamma rays, at low doses, risk estimates based on linearity could be high, and thus regarded as an upper limit. For high LET radiations, such as neutrons and alpha particles, at low doses, risk values may be overestimates or underestimates.

Whatever the logic we may use for a particular mathematical form chosen for a dose-response relationship at very low doses, the inclusion of risk estimates thus derived appears not only appropriate, but essential, if the deliberations of the BEIR Committee are to be used for determining public health policy. Until much more information is available on the mechanisms of radiation carcinogenesis, however, the epidemiological data alone do not help in estimating the precise risk at low doses from data obtained at high doses. The problem, therefore, which must face every expert advisory committee on radiation, is not whether it should include numerical risk estimates, however crude and imprecise, for official documentation, but how it should improve the accuracy of the numerical risk estimates based on epidemiological surveys and laboratory experiments. This is particularly important, since it is now very well known that no matter how carefully the imprecise risk estimates are to be qualified in the text of any official committee report, these numbers are invariably used and quoted by others in and out of context. In such matters of responsible scientific policy, the governmental agencies, the legislative bodies, the regulatory bodies, the radiation-related industries, the consumer advocate groups, and the public media, do not necessarily enjoy the privilege to act irresponsibly, as may be accorded the average uninformed, but concerned citizen. In spite of these inevitable consequences, nevertheless, the 1979 BEIR Report accepted the responsibility to assess the need to establish the most reliable estimate of range of health effects possible in human populations to exposure of low levels of ionizing radiation, in the light of all available knowledge. This decision was necessary, and mainly because certain numerical risk estimates will be used freely in arguments and counterarguments, and often used irresponsibly, in the public forum.

From the dose-response relationships used, and if it is assumed that there is no appreciable effect of dose rate or fractionation of dose, an estimate can be made of the absolute risk of radiation-induced cancer, the major risk of radiation to man. The overall figure derived is about one to five excess cancer cases per million exposed persons per year per rad, depending on the organ or tissue site, with evidence of age-, sex-, and time-dependencies. There are no good reasons to assume, in the determination of risks to health, that each exposed human population is identical, and thus, the risks estimated derived should be the same. Each cohort population in the human experience has a widely identifiable set of variables, there are no identical control popula-

tions. In the case of the human epidemiological surveys of cancer induction by radiation, such biological and physical factors as;initiating and promoting mechanisms, damage to vital biologically active macromolecules, hormonal and immunological imbalances, cellular proliferation, genetically-selected susceptible subpopulations, dose, dose-rate, duration of exposure, physical factors of radiation quality to name just a few, all interact to result in a clinical entity in man which we call cancer (Table 2). The margin for error is large in every case, primarily because of the uncertain nature of the limited data available. Thus, in the estimation of such radiation risks for man, it follows that comparisons of all populations should be made, but only with those data that are considered reliable, and not apt to change significantly over the coming years. However, any generalized summing-up to arrive at a total numerical index of harm based on such limited epidemiological and experimental information without exercising cautious judgement can compound errors inappropriately, and destroy the credibility of the limited interpretation of the reliable epidemiological data that are available.

How Should We Quantitate Our Radiation-Induced Cancer Risk Estimates?

The tissues and organs involved in radiation-induced cancer in man about which we have the most reliable epidemiological data from a variety of sources from which corroborative risk estimates have been obtained include the bone marrow (16, 22-28), the thyroid (22, 23, 28-30), the breast (22, 23, 28, 31-39), and the lung (22, 40-42). The data on bone (22, 28, 43-46) and the digestive organs (22, 23, 25-57) are, at best, preliminary, and do not approach the precision of the others. In several of these tissues and organs, risk estimates are obtained from very different epidemiological surveys, some followed for over 25 years, and with adequate control groups. There is impressive agreement when one considers the lack of precision inherent in the statistical analyses of the case-finding and cohort study populations, variability in ascertainment and clinical periods of observation, age, sex and racial structure, and different dose levels, and constraints on data from control groups.

By far, the most reliable and consistent data have been those of the risk of leukemia, which come from the Japanese A-bomb survivors (22, 42), the ankylosing spondylitis patients treated with x-ray therapy in England and Wales (25-27, 47, 48), the metropathia patients treated with radiotherapy for benign uterine bleeding (51-53), and the tinea capitis patients treated with radiation for ringworm of the scalp (30, 49, 50) (Table 3). There is evidence of an age-dependence and a dose-dependence, a relatively short latent period of a matter of a few years, and a relatively short period of expression, some 10 years. The lifetime risk is of the order of 19 to 28 excess leukemia cases per million exposed persons per rad. This cancer in uniformly fatal (1, 9, 22, 27, 28, 55).

The data available on thyroid cancer are more complex; the surveys include the large series of children treated to the neck and mediastinum for enlarged thymus (28, 29), children treated to the scalp for tinea capitis (30, 40, 50), and the Japanese A-bomb survivors (22) and Marshall Islanders (54) exposed to nuclear explosions (Table 3). Here, there is an age-dependence and sex-dependence--children and females are more sensitive. The lifetime risk is approximately 55 to 162 excess thyroid neoplasms per million exposed persons

Table 2

Human Radiation Carcinogenesis

Some Uncontrolled Variables

1. Initiating and promoting mechanisms
2. Damage to DNA
3. Cellular proliferation
4. Hormonal and immunological imbalance
5. Genetically-predetermined susceptibility
6. Radiation dose and dose rate
7. Duration of exposure
8. Physical factors of radiation quality
9. Lack of controls

Table 3

Risk Estimates of Lifetime Incidence

Radiation-Induced Leukemia and Thyroid Cancer

Tissue-Organ Population	Absolute Risk Estimate of Lifetime Incidence (Cases/10^6/rad)		Dependence
LEUKEMIA			age and dose
Japanese A-bomb Survivors Ankylosing Spondylitis Patients Tinea Capitis Radiotherapy Patients Pelvic Radiotherapy Patients	Males	28	
	Females	19	
THYROID CANCER			age and sex
Neck and Mediastinum Radiotherapy Patients Tinea Capitis Radiotherapy Patients Marshallese Islanders Japanese A-bomb Survivors	Males	55	
	Females	162	

per rad. Although the induction rate is high, the latent period is relatively short, and it is probable that no increased risk will be found in future follow-up. In addition, most tumors are either thyroid nodules, or begign or treatable tumors, and only about 5 percent of the radiation-induced thyroid tumors are fatal (55).

In very recent years, much information has become available on radiation-induced breast cancer in women (22, 31-39) (Table 4). The surveys include primarily women with tuberculosis who received frequent fluoroscopic examinations for artificial pneumothorax, post-partum mastitis patients treated with radiotherapy, and the Japanese A-bomb survivors in Hiroshima and Nagasaki. Here, there is an age- and dose-dependency, as well as a sex-dependency, and the latent period is long, some 20 to 30 years. The estimated lifetime induction rate is about 141 excess cancers per million women exposed per rad. Perhaps about half of these neoplasms are fatal (20, 22, 27, 28, 55).

Another relatively sensitive tissue, and a complex one as regards radiation dose,involving parameters of the special physical and biological characteristics of the radiation quality, is the epithelial tissue of the bronchus and lung (Table 4). The information from the Japanese A-bomb survivors (22-24, 42) and uranium miners in the United States and Canada (40-41), and the ankylosing spondylitis patients in England and Wales (25-27) provide a risk estimate of lung cancer of approximately 39 to 45 excess cancers per million persons exposed per rad. There is some evidence of age-dependence from the Japanese experience and a relatively long latent period. This cancer is uniformly fatal (1, 9, 27, 28, 55).

The lifetime risk of radiation-induced bone sarcoma (Table 4), based primarily on radium and thorium patients who had received the radioactive substances for medical treatment, or ingested them in the course of their occupations (43-46) is low, possibly only 0.05 excess cancer deaths per million exposed persons per rad. For all other tumors arising in various organs and tissues of the body, values are extremely crude and preliminary estimates and probably less than 30 to 50 excess cancers per million exposed persons per rad (Table 5).

There is now a large amount of epidemiological information from various comprehensive surveys from a variety of sources; the most extensive, perhaps, include the Japanese A-bomb survivors (22), the patients treated to the spine for ankylosing spondylitis (25-27, 47-78), the metropathia patients (51, 52), and the early radiologists (56, 57). These data indicate that leukemia is now no longer the major cancer induced by radiation, and that solid cancers are exceeding the relative incidence of radiation leukemia by a factor as high as five (55). That is, in view of the long latent periods for certain solid cancers to become manifest, it can be estimated that perhaps after some 30 years following radiation exposure, the risk of excess solid cancers may prove to be some five times the risk of excess leukemia. This does not necessarily imply that we can readily sum up all the radiation malignancies of the body and neglect the obvious lack of precision of certain of the epidemiological studies, particularly as regards radiation dose distribution, ascertainment, latency periods, and other important physical and biological parameters. The BEIR (1,3), the UNSCEAR (8,9) and the ICRP (10,13) Reports have done this in

Table 4

Risk Estimates of Lifetime Incidence

Radiation-Induced Breast, Lung and Bone Cancer

Tissue-Organ Population	Absolute Risk Estimate of Lifetime Incidence (Cases/10^6/rad)		Dependence
BREAST CANCER TB-Fluoroscopy Patients Mastitis Radiotherapy Patients Japanese A-bomb Survivors	Females	141	age and dose
LUNG CANCER Japanese A-bomb Survivors	Males	39	age
Uranium Miners Ankylosing Spondylitis Patients	Females	45	
BONE CANCER Ra-226 Ingestion Workers Ra-224 Treatment Patients Tinea Capitis Radiotherapy Patients		0.05	age and duration of exposure

Table 5

Risk Estimates of Lifetime Incidence

Radiation-Induced Cancer - Other Cancers

Tissue-Organ Population	Absolute Risk Estimate of Lifetime Incidence (Cases/10^6/rad)		Dependence
Brain, Salivary Glands Stomach, Liver, Colon	Males	21	unknown
	Females	27	
Scalp, *in utero*, neck, spine, Japanese survivors, and pelvis irradiation			
Esophagus, Small Intestine, Rectum, Pancreas, Ovary, Paranasal Sinuses, Lymphoid Tissue Irradiation	Males	39	unknown
	Females	45	

different ways and based primarily on the studies of the Japanese A-bomb survivors (22), and to a much lesser extent, from data on the ankylosing spondylitis patients (25,27), the Metropathia patients (51, 52), the tinea patients (30, 49, 50), and similar epidemiological surveys carefully followed, many of which now have adequate control study populations, a very crude figure of the total lifetime excess absolute risk of radiation-induced cancer deaths can be derived ($\sim$75 to 125 excess cancer deaths/10^6/rad). This figure for all malignancies from low LET radiation, i.e., x-rays and gamma rays, delivered at low doses would be a considerable overestimate of the true risk, and the more accurate value would be less than 100. The actual figure may be as low as 70 excess cancer cases per million persons exposed per rad total lifetime risk, a large fraction of which would not necessarily be fatal (55). This estimated figure remains very unreliable, but it does provide a very rough figure for comparison with other estimates of avoidable risks, or voluntary risks, encountered in everyday life.

What Can We Conclude?

The present scientific evidence and the interpretation of available data can draw very few firm conclusions on which to base scientific public health policy for radiation protection standards. The setting of any permissible radiation level or guide remains essentially an arbitrary procedure (60,61). Based on the radiation risk estimates derived, any lack of precision does not minimize either the need for setting public health policies nor the conclusion that such risks are extremely small when compared with those available of alternative options, and those normally accepted by society as the hazards of everyday life (2, 55, 60, 62). When compared with the benefits that society has established as goals derived from the necessary activities on energy production and medical care, it is apparent that society must establish appropriate standards and seek appropriate controlling procedures which continue to assure that its needs and services are being met with the lowest possible risks (2, 55, 63). This implies continuing decision-making processes in which risk-benefit and cost-effectiveness assessments must be taken into account (2, 58, 61, 62).

The gap between our scientific knowledge and our societal needs appears to be continually widening. In a third of a century of inquiry, embodying among the most extensive and comprehensive scientific efforts on the health effects of an environmental agent, much of the practical information necessary for determination of radiation protection standards for public health policy is still lacking. It is now assumed that any exposure to radiation at low levels of dose carries some risk of deleterious effects. However, how low this level may be, or the probability, or magnitude of the risk, still are not known. Radiation and the public health, when it involves the public health, becomes a broad societal problem and not solely a scientific one, and to be decided by society, most often by men and women of law and government. It is not an exercise in statistical theory or laws of chance. Our best scientific knowledge and our best scientific advice are essential for the protection of the public health, for the effective application of new technologies in medicine and industry, and for guidance in the production of nuclear energy. Unless man wishes to dispense with those activities which inevitably involve exposure to low levels of ionizing radiation, he must recognize that some degree of risk

to health, however small, exists. In the evaluation of such risks from radiation, it is necessary to limit the radiation exposure to a level at which the risk is acceptable both to the individual and to society. A pragmatic appraisal of how man wishes to continue to derive the benefits of health and happiness from such activities involving ionizing radiation in times of everchanging conditions and public attitudes in our resource-limited society is the task which lies before each expert advisory committee on the biological effects of ionizing radiation, now and in future years.

Acknowledgements

The author wishes to acknowledge the many helpful discussions with many of his scientific colleagues, and particularly, those members of expert advisory committees on radiation, which have provided the philosophical approach embodied in his presentation. He acknowledges the scientific papers of numerous authors not listed in the bibliography, since this was not intended as a scientific review of the literature. He is continually grateful to Mrs. Barbara Komatsu for her energy, her patience, her good humor and her expert assistance in the preparation of this manuscript.

References

1. Advisory Committee on the Biological Effects of Ionizing Radiations. National Academy of Sciences - National Research Council. The Effects on Populations of Exposure to Low Levels of Ionizing Radiation, 1979. U. S. Government Printing Office, Washington, D.C., 1979. In press.

2. Advisory Committee on the Biological Effects of Ionizing Radiations, National Academy of Sciences - National Research Council: The Effects on Populations of Exposure to Low Levels of Ionizing Radiation; Washington, D.C., U.S. Government Printing Office, 1972.

3. Advisory Committee on the Biological Effects of Ionizing Radiations, National Academy of Sciences - National Research Council; Considerations of Health Benefit-Cost Analysis for Activities Involving Ionizing Radiation Exposure and Alternatives. EPA 520/4-77-003, National Academy of Sciences, Washington, D.C., 1977.

4. National Academy of Sciences - National Research Council. The Biological Effects of Atomic Radiation. A Report to the Public. National Academy of Sciences - National Research Council, Washington, D.C., 1956.

5. National Academy of Sciences - National Research Council. The Biological Effects of Atomic Radiation. Report of the Committee on the Genetic Effects of Atomic Radiation. National Academy of Sciences - National Research Council, Washington, D.C., 1960.

6. United Nations Scientific Committee on the Effects of Atomic Radiation. Report of the United Nations Scientific Committee on the Effects of Atomic Radiation. Supplement No. 17 (A/3838). United Nations, 1958.

7. United Nations Scientific Committee on the Effects of Atomic Radiation. Report of the United Nations Scientific Committee on the Effects of Atomic Radiation. Supplement No. 14 (A/5814). United Nations, New York, 1964.

8. United Nations Scientific Committee on the Effects of Atomic Radiation. Ionizing Radiation: Levels and Effects. United Nationa, New York, 1972.

9. United Nations Scientific Committee on the Effects of Atomic Radiation. Sources and Effects of Ionizing Radiation. United Nations, New York, 1977.

10. International Commission of Radiological Protection. The Evaluation of Risks from Radiation. A Report Prepared for Committee I of the International Commission of Radiological Protection. ICRP Publication 8. Pergamon Press, Oxford, 1966.

11. International Commission on Radiological Protection. Recommendations of the International Commission on Radiological Protection. (September 17. 1965). ICRP Publication 9. Pergamon Press, Oxford, 1966.

12. International Commission of Radiological Protection. Radiosensitivity and Spatial Distribution of Dose. ICRP Publication 14. Pergamon Press, Oxford, 1969.

13. International Commission on Radiological Protection. Radiation Protection. ICRP Publication 26. Recommendations of the International Commission on Radiological Protection. (Adopted January 17, 1977) Pergamon Press, Oxford, 1977.

14. National Council on Radiation Protection and Measurements. NCRP Report No. 39. Basic Radiation Protection Criteria. National Council of Radiation Protection and Measurements, Washington, D.C., 1971.

15. National Council of Radiation Protection and Measurements. NCRP Report No. 43. Review of the Current State of Radiation Protection Philosophy. National Council on Radiation Protection and Measurements, Washington, D.C., 1975.

16. Medical Research Council. The Hazards to Man of Nuclear and Allied Radiations. Her Majesty's Stationery Office, London, 1956.

17. Reactor Safety Study. An Assessment of Accident Risks in U.S. Commercial Nuclear Power Plants. Appendix VI. United State Nuclear Regulatory Commission, Wash-1400, NUREG-75/014, Washington, D.C., October 1975.

18. Brown, J.M. Linearity vs. non-linearity of dose response for radiation carcinogenesis. Health Phys. 31: 231-245, 1976.

19. Brown, J.M. The Shape of the Dose-Response Curve for Radiation Carcinogenesis. Extrapolation to Low Doses. Radiation Res.71: 34-50, 1977.

20. Upton, A.C. Radiobiological effects of low doses: Implications for radiobiological protection. Radiation Res. 71: 51-74, 1977.

21. Land, C.E. Strategies for epidemiologic research on the effects of low-level radiation. Presented at the AAAS Annual Meeting, Symposium on Epidemiology Studies of Low-Level Radiation Exposure, Houston, Texas, January 3-8, 1979.

22. Beebe, G. W., Kato, H. and Land, C. E. Mortality Experience of Atomic Bomb Survivors 1950-1974. Life Span Study Report 8. Radiation Effects Research Foundation Technical Report RERF TR 1-77, National Academy of Sciences, Washington, D.C., 1977.

23. Mole, R. H. Ionizing radiation as a carcinogen; practical questions and academic pursuits. Brit. J. Radiol. 48: 157-169, 1975.

24. Moriyama, I. M. and Kato, M. Mortality experience of A-bomb survivors 1950-1972. Atomic Bomb Casualty Commission Report ABCC-15-73., 1973.

25. Court Brown, W. M. and Doll, R. Mortality from cancer and other causes from radiotherapy for ankylosing spondylitis. Brit. Med. J. 2:1327-1332,

1965.

26. Smith, P.G. and Doll, R. Age and time dependent changes in the rates of radiation induced cancers in patients with ankylosing spondylitis following a single course of x-ray treatment. (In) International Symposium on the Late Biological Effects of Ionizing Radiation, IAEA-SM-224/711, Vienna, 13-17 March, 1978, In press.

27. Doll, R. and Smith, P. G. Causes of death among patients with ankylosing spondylitis following a single treatment course with x-rays. To be published.

28. Pochin, E. E. Radiology now. Malignancies following low radiation exposures in man. Brit. J. Radiol. 49: 577-579, 1976.

29. Hempelmann, L. H., Hall, W. J., Phillips, M., Cooper, R. A. and Ames, W. R. Neoplasms in persons treated with x-rays in infancy: Fourth survey in 20 years. J. Natl. Cancer Inst. 55: 519-530, 1975.

30. Modan, B., Baidatz, D., Mart, H., Steinitz, R., and Levin S. G. Radiation-induced head and neck tumours. Lancet 1: 277-279, 1974.

31. Myrden, J. A. and Hiltz, J. E. Breast cancer following multiple fluoroscopies during artificial pneumothorax treatment of pulmonary tuberculosis. Canadia Med. Assoc. J. 100: 1032-1034, 1969.

32. Mettler, F. A., Hempelmann, L. H., Dutton, A. M., Pifer, J. W., Toyooka, E. T., and Ames, W. R. Breast neoplasms in women treated with x-rays for acute post partum mastitis. A pilot study. J. Natl. Cancer Inst. 43: 803-811, 1969.

33. Myrden J. A. and Quinlan, J. J. Breast carcinoma following multiple fluoroscopies with pneumothorax treatment of pulmonary tuberculosis. Ann. Roy. Coll. Physicians Can. 7: 45-51, 1974.

34. Upton, A. C., Beebe, G. W., Brown, J. M., Quimby, E. H. and Shallabarger, C. Report of NCI ad hoc working group on the risks associated with mammography in mass screening for the detection of breast cancer. J. Natl. Cancer Inst. 59; 480-493, 1977.

35. McGregor, D. H., Land, C. E., Choi, K., Tokuoka, S., Lui, P., Wakabayahi, T. and Beebe, G. W. Breast cancer incidence among atomic bomb survivors, Hiroshima and Nagasaki, 1950-1969. J. Natl. Cancer Inst. 50: 799-811, 1977.

36. Boice, J. D., Jr. and Monson, R. R. Breast cancer in women after repeated fluoroscopic examinations of the chest. J. Natl. Cancer Inst. 59: 823-832, 1977.

37. Shore, R. E., Hempelmann, L. H. Kowaluk, E., Mansur, P. S., Pasternak, B. S., Albert, R. E. and Haughie, G. E. Breast neoplasms in women treated with x-rays for acute post-partum mastitis. J. Natl. Cancer Inst. 59: 813-822, 1977.

38. Baral, E., Larsson, L. E. and Mattsson, B. Breast cancer following irradiation of the breast. Cancer 40: 2905-2910, 1977.

39. Mole, R. H. The sensitivity of the human breast to cancer induction by ionizing radiation. Brit. J. Radiol. 51: 401-405, 1978.

40. Health Effects of Alpha-Emitting Particles in the Respiratory Tract. Report of ad hoc Committee on "Hot Particles" of the Advisory Committee on the Biological Effects of Ionizing Radiations. National Academy of Sciences, Washington, D.C., 1976.

41. Ham, J. M. Report of the Royal Commission on the Health and Safety of of Workers in Mines. Ministry of the Attorney General, Province on Ontario, Toronto, Canada 1976.

42. Ishimaru, T., Cihak, R. W., Land, C. E., Steer, A., and Yamada, A. Lung cancer at autopsy in A-bomb survivors and controls, Hiroshima and Nagasaki. Cancer 36: 1723-1728, 1975.

43. Mays, C. W., Spiess, H., Taylor, G. N., Lloyd, R. D., Jee, W. S. S., McFarland, S. S., Taysum, D. H., Brammer, T. W., Brammer, D., and Pollard, T. A. Estimated risk to human bone from ^{239}Pu. (In) Health Effects of Plutonium and Radium, W. S. S., Jee, Ed., pp. 343-362, J. W. Press, Salt Lake City, Utah, 1976.

44. Rowland, R. E. and Stehney, A. F. Radium-induced malignancies (In) Argonne National Laboratory Report ANL-77-65, Part II, 206-210, 1977.

45. Mays, C. W. and Spiess, H. Bone sarcoma risks to man from ^{224}Ra,^{226} Ra and ^{239}Pu. (In) Biological Effects of ^{224}Ra. Benefit and Risk of Therapeutic Application. Miller, W. A. and Ebert,H. G., eds. pp. 168-181 Nyhoff Medical Division, The Hague, 1978.

46. Mays, C. W., Spiess, H., and Gerspach, A. Skeletal effects following ^{224}Ra injections into humans. Health Phys. 35: 83-90, 1978.

47. Smith, P. G., Doll, R. and Radford, E. P. Cancer mortality among patients with ankylosing spondylitis not given x-ray therapy. Brit. J. Radiol. 50: 728-734, 1977.

48. Radford, E. P., Doll, R. and Smith, P. G. Mortality among patients with ankylosing spondylitis not given x-ray therapy. New Eng. J. Med. 279: 572-576, 1977.

49. Modan, B., Ron, E. and Werner, A. Thyroid cancer following scalp irradiation. Radiology 123: 741-744, 1977.

50. Shore, R. E., Albert, R. E. and Pasternak, B. S. Follow-up of patients treated by x-ray epilation for tinea capitis. Arch. Environ. Health 31: 21-28, 1976.

51. Doll, R. and Smith, P. G. The long term effects of x-irradiation in patients treated for metropathia haemorrhagica. Brit. J. Radio. 41: 362-368, 1968.

52. Smith, P. G. and Doll, R. Late effects of x-irradiation in patients for metropathia haemorrhagica. Brit. J. Radiol. 49: 224-232, 1976.

53. Doll, R. Cancer following therapeutic external irradiation. (In) Clark, R. L., Cumley, R. W., MaCay, J. E., and Copeland, M. M., eds. Oncology 1970: Proceedings of the Tenth International Cancer Congress. Vol. 5, Environmental Causes, pp. 1-28, Year Bood Medical Publ., Chicago, Ill,1970.

54. Conard, R. A. Summary of Thyroid Findings in Marchallese 22 years after exposure to radioactive fallout in radiation-associated thyroid carcinoma. (In) DeGroot, L. J., ed. Radiation-Associated Thyroid Carcinoma, pp. 241-257, Academic Press, New York, 1977.

55. Pochin, E. E. Why be quantitative about radiation risk estimates? Lauriston S. Taylor Lectures. No. 2. National Council of Radiation Protection and Measurements, Washington, D.C., 1978.

56. Seltzer, R. and Sartwell, P. E. The influence of occupational exposure to radiation on the mortality of American Radiologists and other medical specialists. Am J. Epidemiol. 81: 2-22, 1965.

57. Matanoski, G. N., Seltzer, R., Sartwell, P. E. et. al. The current mortality rates of radiologists and other physician specialists: specific causes of death. Amer. J. Epidemiol. 101: 119-210, 1975.

58. International Commission on Radiological Protection. Problems Involved in the Development of an Index of Harm. ICRP Publication 27. Pergamon Press, Oxford, 1978.

59. Pochin, E. E. Estimates of industrial and other risks. J. Roy. Coll. Phys. Lond. 12:]10-]14, 1978.

60. Comar, C. L. An individual looks at the implications of the BEIR Report. Practical Radiol. 1: 40-44, 1973.

61. Fabrikant, J. I. Benefit-cost analysis in diagnostic radiology. (In) Panel on Efficiency, Cost-Benefit Analysis and Health Resource Allocation in Radiology. James Picker Foundation Conference. The Radiologist in Society ---Prospects and Problems for the 1980s. Key Biscayne, Florida, April 1977.

62. Fabrikant, J. I. Benefit-csot analysis for diagnostic radiology in medicine. (In) Symposium on Risks and Benefits in Medical Radiation Applications. XIV Intern. Congr. of Radiology, Rio de Janeiro, Brasil, October 23-29, 1977.

63. Fabrikant, J. I. Perspectives of decision-making and estimation of risk in populations exposed to low levels of ionizing radiation. Presented at the AAAS Annual Meeting, Symposium on Epidemiology Studies of Low-Level

Radiation Exposure, Houston, Texas, January 3-8, 1979. Report LBL-8667, pp 1-40, Lawrence Berkely Laboratory, University of California, Berkeley, California, January 1979.

64. International Commission on Radiation Protection Implications on Commission Recommendations that Doses be Kept as Low as Readily Achievable. ICRP Publication 22, Pergamon Press, Oxford, 1973.

Question: Do you think you could say that a single rad of irradiation would produce any form of malignancy or one rad piled on top of rads would produce it?

Dr. Fabrikant: Do you mean one additional rad or one rad of radiation?

Question: One rad of radiation.

Dr. Fabrikant: One rad of radiation probably can induce a neoplasm after a number of years, if a large enough population is exposed. But it has to be a large population exposed because the probability is small. To an individual, the risk is almost negligible.

Question: They just have to live a long time.

Dr. Fabrikant: A very large number of persons would have to be exposed, and this population would have to live a long time.

Comparisons with Medical Exposures and Thyroid Uptake Implication

Jack S. Krohmer, Ph.D.

We all realize that the reason we are here is our concern over the TMI accident. It is obvious that one of the things that is bothering everyone is the controversy over the effects of low level radiation. My particular part in this program is to speak to a comparison of the accidental radiation exposure from TMI with purposeful medical radiation exposure for diagnostic purposes.

It should be of interest to all of you that the Federal Government, through the President, last year became concerned over just these questions and by a letter dated May 9, 1978, formed an interagency task force(Table 1). The President called for some joint efforts by the various agencies of the government to try to straighten out some of the problems, the sort of problems we are concerned with following TMI, regarding health effects of ionizing radiation. It is of interest to note that the task group was formed ahead of time and its draft report was issued on February 20, 1979, some 36 days before the TMI incident. It is unfortunate that it hadn't come out much earlier, and that what the report projects to do hadn't already been done. The chairman of the Interagency Task Force was F. Peter Libassi, who is the general counsel for HEW and the report in its little more than a month of existence has come to be known as the Libassi Report.

The Libassi Report includes coverage of medical and dental exposure, as well as the risk of living near a nuclear power plant. Table 2 lists some of the messages that came out of this report. They are very interesting to note, in view of the TMI incident and in view of your interest in coming to this seminar.

The first message states that low level background radiation is a part of the earth's natural environment. When we are talking about low level radiation, it is not something that is completely new to the population of the United States or the world. Second, it was the conclusion of this interagency group that a message that should get across to the public is that the degree of risk associated with exposure to low level ionizing radiation is very low. The question is, how low? That comes out in the third message, which indicates that scientists are in disagreement about the precise magnitude of risk. You have heard some of these views in this seminar today, but our knowledge is somewhat better than you might gather just from the surface. The fourth message is that unnecessary radiation exposures should be avoided. As I mentioned in the press conference this morning, I've spent 32 years in the radiation field, all in or associated with the medical field, and I have never known anybody in that field that did not feel this way. Avoiding unnecessary exposure is no new idea and has never been. The fifth message is extremely important and has been brought up earlier; it is that any risk from radiation must be balanced against the benefit it provides. Dr. Fabrikant talked about this concept. The BEIR committee is interested in comparing possible risks against the benefits provided by the radiation related activities. In such comparisons, it is important to keep radiation risk in perspective with other risks from environmental hazards and from other human activities.

Table 1

INTERAGENCY TASK FORCE ON
THE HEALTH EFFECTS OF IONIZING RADIATION

Created at the direction of the White House in a letter dated May 9, 1978.

Coordinated by the Secretary of Health, Education and Welfare.

Includes representatives from:

THE DEPARTMENT OF ENERGY
THE DEPARTMENT OF DEFENSE
THE DEPARTMENT OF LABOR
THE VETERANS ADMINISTRATION
THE ENVIRONMENTAL PROTECTION AGENCY
THE NUCLEAR REGULATORY COMMISSION
in addition to
THE DEPARTMENT OF HEALTH, EDUCATION & WELFARE

Draft report issued on February 20, 1979, about one month before the start of the THREE MILE ISLAND incident.

CHAIRMAN OF TASK FORCE: F. Peter Libassi, General Counsel, H.E.W.

Report included coverage of: MEDICAL and DENTAL EXPOSURE
RISK OF LIVING NEAR NUCLEAR POWER PLANTS

Table 2

MESSAGES OF LIBASSI REPORT

1. Low-level background radiation is a part of the earth's natural environment.

2. The degree of risk associated with exposure to low-level ionizing radiation is very low.

3. Scientists are in disagreement about the precise magnitude of this risk.

4. Unnecessary radiation exposure should be avoided.

5. Any risk from radiation must be balanced against the benefits provided by radiation-related activities and must be kept in perspective with other risks from environmental hazards and from other activities.

****

PROBLEMS IN DESIGNING ADEQUATE PUBLIC INFORMATION PROGRAMS

1. There is substantial disagreement among experts on the extent of risk resulting from exposure to low levels of radiation.

2. The language in which radiation exposure is discussed is technical and difficult for the average person to understand.

3. Within the federal government there is a lack of information coordination.

****

The Interagency Task Group indicated (Table 2) that there would be difficulties in getting these messages across to the public. We have seen these come up in the last few weeks. First, the disagreement between experts as to the extent of risk resulting from exposure to low level ionizing radiation is present and it does cause a problem. Second, the language in which radiation exposure is discussed is technical and difficult for the average person to understand. We saw this difficulty so strongly in the reports in the Press; they are members of the public and we got to see what they write. In the reports that came out during the TMI incident, it really shocked me to hear the terms "radiation" and "radioactivity" used interchangeably. There is a difference. Granted, radiation is emitted from radioactive materials, but the radioactive materials remain in a vicinity for some time and do continue to emit radiation. The public has the feeling that radiation itself wanders around and continues to expose individuals. I flew back from vacation, where I was when this incident occurred, with a woman who said "How long does that "radiation" stay in your body?" It was obvious that what she was really talking about was "radioactivity", but she said "radiation". I told her that radiation generally travels at 186,000 miles a second and that by the time she thought about it, it had long since arrived at wherever it was going. It is unfortunate that such misunderstandings have occurred. I also noticed that the reports I read stated that the measurements with total body counters on individuals indicated that there was no "radiation" left in the patient. They really meant "radioactive materials". I think all of us have to be somewhat careful in our reporting and language.

It is interesting that solutions to this problem were suggested by the Interagency Task Group before this incident occurred. They recommended that public information programs be developed to include the type of information listed in Table 3. They suggested that we (1) clearly describe complex concepts of comparative risks, possible risks and acceptable risks and that we (2) outline the scientific basis for risk estimates and explain why such estimates are difficult to make for any given individual (or for large numbers of people). The parentheses I added to their words, because this is an additional problem. It is not simple to even get the risks at low level for large populations; for individuals, it becomes an impossibility.

The third recommendation is quite important; that is, to describe the distinction between risk and certainty. I think that most people, when they hear that there may be 100 additional cancer deaths due to the exposure of a population group to 1 rad over the course of their lifetimes, expect to see these individuals laid out somewhere. This is not the case. We are talking about a possible risk and not a certainty. If we apply the probabilities to very large populations, the result gets closer to certainty but it is still not certain.

The fourth suggestion is to describe carefully and clearly the contextual meaning of terms used to describe radiation doses and exposures; for instance, delineation of high and low level radiation doses. The statement on the bottom of Table 3 states that to assist individuals in making decisions about themselves, information specialists and scientists must cooperate to develop an explanation of radiation risk in terms that are meaningful to the average person, information that will attempt to satisfy both the need for scientific accuracy and the need for simplicity.

Table 3

INFORMATION TO BE DEVELOPED

1. CLEARLY DESCRIBE THE COMPLEX CONCEPTS OF:

   COMPARATIVE BENEFITS
   POSSIBLE RISK
   ACCEPTABLE RISKS

2. OUTLINE THE SCIENTIFIC BASIS FOR RISK ESTIMATES AND EXPLAIN WHY SUCH ESTIMATES ARE DIFFICULT TO MAKE FOR ANY GIVEN INDIVIDUAL (or for large numbers of people)

3. DESCRIBE THE DISTINCTIONS BETWEEN RISK AND CERTAINTY.

4. DESCRIBE CLEARLY AND CAREFULLY THE CONTEXTUAL MEANING OF TERMS USED TO DESCRIBE RADIATION DOSES AND EXPOSURES, PARTICULARLY WHEN THOSE TERMS ARE USED RELATIVE TO EACH OTHER SUCH AS "HIGH" OR "LOW".

The Libassi report states that " To assist individuals in making their decisions, information specialists and scientists must cooperate to develope an explanation of radiation risks in terms that are meaningful to the average person, and that will attempt to satisfy both the need for scientific accuracy and the need for simplicity.".

THAT IS THE OBVIOUS AND STATED REASON FOR HOLDING THIS SPECIAL SEMINAR !!

The need for better information is obvious and it is the stated reason for holding this conference for a group of people who are certainly, on the average, more highly educated than the average in the general population. This need was set forth before the accident even occurred, and I think it is very important and I hope that the government continues to work toward this goal. Many of us in the field have said for a long time that some of the monies that are spent by the Federal Government on the problems of low level ionizing radiation could be well spent on educating the general public so that they will have a better understanding of what goes on. Unfortunately, those of us who have been in the field for a number of years have made a statement that is true, but I think it is the one that causes a lot of problems, i.e., "You can't see, hear, feel, taste or smell radiation". Now you can't do that with ultraviolet radiation either, and there are other things, such as asbestos, that fit into the same category, however, the statement puts radiation into a completely mysterious situation. I think this is what causes the public to worry excessively, in addition to the fact that they don't have all of the information that they really should have.

Now, let's talk about some of the things that were in the messages that were to be delivered. First, natural background radiation. I don't know how many of you are aware of the very wide range of natural background levels that are present around the world and the populations that are exposed to them. In Table 4, the top 4-5 lines pertain to the U.S.A.; we've heard most of those this morning. The Atlantic and Gulf coast areas have background levels something of the order 65 to 70 millirem per year. This includes contributions from cosmic radiation, terrestrial radiation and internal radioactivity which adds to the radiation dose. The dose for the non-coastal plains (which constitute most of the U.S.A.) is a little higher and also there are more people there. (Incidentally, this is not the only population that there is, if you add these figures together, you don't get the U.S. population. The table shows only the groups that were included in the areas where the background levels are given). The background is 80 to 95 millirem per year for the non-coastal plains. For the Colorado plateau which has a population of 1,070,000 people with most in Denver, the background level is higher, about 125 to 160 millirems. This happens because the altitude is such that there is not much shielding from the atmosphere for cosmic radiation so the cosmic radiation levels are higher and also the terrestrial elements are such that the terrestrial radiation is higher. The highest spot in the United States where there is a significant number of people is Leadville, Colorado, which has a background level of 235 millirems/yr. Leadville has a population of about 10,000 and an elevation of 10,000 feet; the main reason for the difference between Denver and Leadville is that extra 5,000 ft. of elevation. There are areas in Central Florida, high phosphate areas, where the terrestrial radiation is high enough to bring the level up to something like 200 millirems per year.

Outside the U.S.A, we find some rather startling numbers, coastal strips of Brazil, where approximately 30,000 people live and the background radiation level is 500 millirem per year. In France, granite rock areas, 7,000,000 people, 180 to 350 millirems/yr. considerably above U.S. levels. In India, the Kerala and Madras states, 1300 millirems per year and that is for 100,000 people. That value of 1300, happens to be 20 times as high as

Table 4

NATURAL BACKGROUND LEVELS

AREA	POPULATION INCLUDED	BACKGROUND LEVEL (mrem/yr)
U.S. (Atlantic & Gulf Coast)	6,760,000	65 - 70
U.S. (Non-coastal plains)	46,780,000	80 - 95
U.S. (Colorado Plateau)	1,070,000	125 - 160
U.S. (Leadville,Colorado)	10,000	235
U.S. (Central Florida & New England Areas)	?	200
Brazil (Coastal strips)	30,000	500
France (Granite rock areas)	7,000,000	180 - 350
India (Kerala & Madras states)	100,000	1300
Niue Island (Pacific)	3,000	1000
Egypt (Northern Nile Delta)	Densely Populated	300 - 400
World (Calculated average)	2 billion	80 - 90

the low value of 65. Niue, an island in the Pacific, not many people there, has a background exposure level of 1000 millirems/yr. Egypt and the Northern Nile delta, 300-400 millirems per year for a very large population. The world calculated average exposure over 2 billion persons is about 90 millirems/yr. Now this doesn't prove anything in itself, but it does turn out that in spite of a factor of 20 difference in exposure, to the present time, there have not been noted any great differences in genetic effects, carcinogeneity and so forth. This indicates that differences by a factor of 20 doesn't seem to make differences in population risks and nobody has felt that there is enough difference to ask people to move out of Denver, move out of the Kerala state, and so forth. So, the background radiation level is not just a simple number like 80 to 95 millirems, but rather, if you consider the world's population, it varies over a factor of something of the order of 20 and no one has proven risk differences as yet.

Let us go on to the second thing that was mentioned, that there is a disagreement as to the risks. In Table 5, I have tried to tie together some estimated risks from radiation exposure. I didn't have the benefit of the BEIR 1979 report, the risk estimates came from the 1972 BEIR report. I listened to Dr. Fabrikant today and, if anything, I think that I heard that the risk numbers are lower in the new report. Spontaneous genetic mutations are assumed to be something like 30,000 or more per million per year. The UNSCEAR 1972 report, using a mutation doubling dose of 100 rems comes up with the estimate that 1 rem of exposure will yield a 1% increase over spontaneous effects. As I understand it, they took into account a low dose rate effect in arriving at the number of 100 rads as the doubling dose. The same year, the BEIR committee arrived at figures of from .5 to 5 percent and this arose from doubling dose estimates of 20 rads which would give you the 5% number to 200 rads, which would give you the 0.5% number. Dose rate was not taken into effect. As I understand from Dr. Abrahamson's presentation, the estimates for doubling dose now are taken as 50 to 250 instead of 20 to 200 rems. This doesn't change things greatly.

The spontaneous rate of cancer induction (deaths) including leukemia per million is something like 1,750 per year. For a 200,000,000 population in the U.S., that is about 350,000 cancer deaths per year. The increase in cancer deaths per rem would be 0.4%, that is about 7 extra cancer deaths per million population. Dr. Fabrikant said 1 to 5 this morning. Apparently, BEIR 1979 has dropped its previous estimate somewhat. These estimates are for acute dose, i.e., all of these estimates have to do with a single dose of 1 rem in a short period of time and with 25 years of observation.

The other estimate of 1% increase in cancer deaths relates to a continuous 1/10th of a rem per year exposure over a 25 year period. According to the 1972 BEIR report, this 1% increase would mean some 17 or 18 additional deaths due to cancer per year per million people.

Now let us consider thyroid cancer induction. It should be emphasized these are cases, not deaths, because thyroid cancer does not always lead to death; it actually has a relatively low mortality and a long latency period. The spontaneous rate in 1970 was 44 cases per million, per year of thyroid cancer, which amounted to 5.25 cancer deaths per year. About 1 out of 8

Table 5

"ESTIMATED" RISKS FROM RADIATION EXPOSURE OF 1 rem

EFFECT CONSIDERED	SPONTANEOUS RATE PER MILLION	% INCREASE PER rem	SOURCE	REMARKS
Genetic mutations	30,000/yr	1.0	UNSCEAR	Takes low dose rate into account
Genetic mutations	30,000/yr	0.5 - 5.0	BIER	Low dose rate not considered
Cancer Induction(Deaths) (including leukemia)	1,750/yr	0.4	BIER	Single acute dose 25 yr observation
	1,750/yr	1.0	BIER	Continuous 0.1rem per yr over 25 yr
Thyroid Cancer Induction (Cases, not Deaths)	44/yr (5.25 deaths)	5.7 - 21	BIER	Long latency & low mortality

NOTES: Percent increase per rem estimated from extrapolation from data for acute doses of 25 rems and above.

SOURCES: UNSCEAR= United Nations Scientific Committee on Effects of Atomic Radiation (1972).

BIER= Advisory Committee on the Biological Effects of Ionizing Radiation (November 1972), National Research Council.

thyroid cancer patients succumb to that disease. The estimates of percent increase in thyroid cancer cases per rem ranges from 5.7 to 21%; the 21% represents about 9 cases per year per million and a little over 1 death per million for a 1 rem exposure to the thyroid glands of a population.

Most of this data in Table 5 has been extrapolated using non-threshold, linear extrapolation and most of it comes from data for acute exposures at 25 rems and above. We have heard a lot about linear extrapolation and non-threshold assumptions in previous presentations today. We also keep hearing that we don't know what the effects of low level radiation are. We don't know in certainty but the feeling of most people on committees such as BEIR, UNSCEAR, the ICRP, NCRP and so forth, is that the figures that are extrapolated using the non-threshold linear extrapolation are probably over-estimates. The following quote from NCRP Report Number 43, dated 1975, relates to this feeling and is a review of the current state of radiation protection philosophy. It states, "All national and international groups which have studied the problem of quantitative carcinogenic risk estimates have regarded the practice of linear extrapolation as over-estimating the risk when the extrapolation is made from the rising and fairly linear portion of the dose effect relationship." Now one thing which Dr. Fabrikant didn't say, I think he just assumed that we knew, is that one of the points that is supposed to be on that linear curve is one at zero. We assume that if there is no dose, there is no effect. So you tie that point down and extrapolate.

A second quote from the same source speaks to some of the papers that suggest that carcinogenic risk per unit dose at low doses is greater than obtained by the linear extrapolation process. These papers were presented in 1975 and we have heard about them today. The quote states, "The suggestion that carcinogenic risk per unit dose at low doses is greater than that obtained by linear extrapolation from the rising portion of an observed dose-effect curve runs counter to other opposing concepts, including the well-supported concept of multi-event mechanisms for most if not all types of cancer. It seems probable, for example, that if there are indeed cancers induced by small doses of radiation, they occur only in a relatively small number of highly susceptible individuals, and with factors other than radiation predominating."

Now let's talk about medical radiation, which is deliberately given to patients to obtain diagnostic information. Table 6 shows some data that I have put together, based on HEW publication 76-8030 entitled, "Radiation doses from diagnostic x-ray studies." There is a little bit in this figure from the Libassi report and some from the EPA 1972 report. For one thing, as you may have noted from my summary, to try to compare the effects from accidental exposure (such as we get from the TMI incident) and that from medical radiation exposure is not really fair. It is like comparing thievery with solicitation of funds for a charity. What is different? First, medical radiation is given for the benefit of the individual who is being exposed. I know that there will be some people in the audience that can pick at that and cite examples of unnecessary diagnostic exposure of individuals. But for the most part, if done properly and that is what we are all trying to do, medical x-ray exposure is given for benefit and its benefit is to the individual being exposed. Second, the medical exposures are generally

Table 6

USUAL DOSES FOR MEDICAL EXPOSURES

PROCEDURE	DOSE TO SELECTED SITES (mrem)				
	SKIN	THYROID	BONE MARROW	GONADS	EMBRYO
Chest X-ray (PA)	30	1.2	3.1	0.05	0.03
Chest X-ray (Lateral)	50	5.8	2.2	0.05	0.10
Thoracic Spine X-ray(AP)	500	59.5	21.5	0.90	0.70
Thoracic Sp. X-ray (Lat)	1000	8.9	28.0	0.40	0.40
Skull X-ray (AP)	100	30.5	1.4	-	-
Skull X-ray (Lateral)	100	13.9	3.8	-	-
Pelvis X-ray (AP)	500	-	23.5	131	176.5
Pelvis X-ray (Lateral)	1000	-	33.0	73	56
Pelvis Fluoroscopy	7000	-	100	786	1059
Lumbar Spine X-ray(AP)	1000	-	46	238	309
Lumbar Spine X-ray(Lat)	2000	-	54	116	78
Upper G.I. Series	900	100	530	170	100
Barium Enema Series	1000	-	870	900	1170
Thyroid Uptake (I-131) (10 microcuries)	-	30,000	35	45	NA

NOTES: Above data derived from HEW Publication 76-8030, Libassi report & 1972 EPA report

limited to a small portion of the body. When we are talking about accidental exposure, e.g., the TMI incident, we are talking, for the most part, about total body radiation. When we evaluate medical exposure, we have to divide it up into exposures to various body organs. Also, what you generally hear quoted for exposures from medical uses of radiation are skin doses. Those are entrance doses and have a higher numerical value than the actual organ doses which are most closely linked to radiation risks.

The organ exposures or doses listed in Table 6 for various diagnostic procedures were prevalent when we were using old types of screens. There are now some types of intensifying screens that are coming into quite widespread use which cut the dose down to about 1/2, without losing significant amounts of information. The organs at risk that are of interest include: the thyroid, which seems to be a very susceptible organ, the bone marrow, where the blood forming cells are located, the gonads and the embryo, if present. The bone marrow has to do with the production of leukemia and bone cancer. The gonads are included because we are concerned with genetic effects which some years ago were thought to be the most important effects, but are not now thought to be. Lastly, the embryo is included for assessing the teratogenic effects. I have included doses to the embryo in these columns, but for the most part, studies will not be carried out if it is known that the patient is pregnant. Diagnostic x-rays that expose the embryo to significant amounts of radiation (pelvic x-ray, pelvic fluoroscopies, lumbar spinal, GI series or barium enemas) are not done unless absolutely necessary for the life of the mother and the fetus.

The largest organ dose you will note in Table 6 is 30,000 millirem or 30 rems to the thyroid gland with the usual thyroid uptake study using 10 microcuries of Iodine-131. I calculated that number assuming a dose of 10 microcuries, a gland size of 20 grams and a 50% uptake. It is not a small dose. This diagnostic test has been done for some time but an incidence of thyroid carcinoma after these doses has never been shown. In the treatment of hyperthyroidism, the dose goes up to about 10,000 to 15,000 rems, and in this situation the incidence of thyroid carcinoma is below the normal incidence probably because the cells in which thyroid carconoma take place are not there anymore.

The dose to bone marrow and gonads from most diagnostic procedures as shown in Table 6 are fairly low. These are the sorts of numbers that individuals are expected to look at in order to evaluate the risk from the procedure. Most individuals who evaluate exposure data do so to compare procedures, but do not use the data to limit exposures if the diagnostic procedures are indicated. In this case, the possible benefits far outweigh any risks.

In determining the average important medical exposure in the U.S., what has been done is to take the bone marrow doses from medical exposures and to obtain an average, as based upon the frequency of use of the various procedures. This number is estimated to be something of the order of 100 millirems per year to an average member of the U.S. population. The second average number commonly used is the genetically significant dose (GSD) which is derived from the gonad doses in Table 6. For the U.S. population, the

genetically significant dose is presently of the order of 20 millirems per average individual. Incidentally, there was a big mistake in the past in that number; it was wrongly estimated in 1964 at 55 millirems. It is my opinion that the Radiation for Health and Safety Law of 1968 was passed with an awful lot of influence coming from that wrong number because that number happened to be higher than that for any of the advanced nations of the world. Their values were all less than 55 millirems and it is not surprising that Congress wondered how come we, who are more advanced than other countries, have a higher dose? Testimony to this effect was used to pass the law and I have a feeling that if the right figure was known, a lot of the adverse influence would have disappeared. It turned out that our number, at that time, was 18 millirem, a value that was about the lowest in the world, instead of the highest. Many people don't know this; as a matter of fact, the primer for this seminar has the number 55 in it, again the wrong number from the 1964 study.

The number that is ordinarily quoted is 100 millirems per year from medical exposure. Keep in mind that this includes many people, a number of people who have had no exposure, as well as many people who have had chest x-rays (the most common examination but for which exposures are quite low). I have looked into the statistics for many hospitals and have found that 50% to 75% of the x-ray procedures carried out in most hospitals are chest x-rays. So, there are a lot of people who have low exposures. Then there are smaller numbers of people with high exposure studies, but these tend to be older people. Therefore, the average of 100 millirems to a number of the population of the U.S. is a number that, to an individual, can't really mean very much, and as I stated in my summary, probably shouldn't mean too much because of the fact that the benefit without any doubt exceeds the risk and also the benefit and the risk are to the same person.

In Table 7, I put together some data on external and internal exposures from the TMI accident and the associated risks. I was waiting for Dr. Wald to come with the official data from the government agencies. It is no more official than what I got about a week ago and these numbers may look very familiar to you. There were 166,000 people in the 10 mile radius, whereas, 2,650,000 includes everyone out to 50 miles. Now, if we run a weighted risk estimate for this distribution of external man-rem exposure to the 2.65 million people, then we get an estimate of an additional .011 deaths per year in that population. That is based on the risk figures that I had from the 1972 BEIR report. If the official exposure estimate increases, the risk will also increase proportionately.

With regard to internal exposure, the number that I felt was most important was the number of picocuries of Iodine-131 per liter of milk. (Note: A picocurie is one-millionth of a microcurie). The radioactive Iodine-131 gets in the milk from the plume, from fallout inhaled by animals or possibly absorbed from grass eaten by animals and then eventually getting into their milk. I would rather use this number and not the iodine on the grass or in the plume. I think this preferable because it is like counting centipedes rather than counting centipedes' legs and dividing by 100. I used that number of 35 picocuries of Iodine-131/liter of milk and assumed that for 7 days some child drank 2 liters of milk per day. Considering that a child

Table 7

EXTERNAL DOSES (Integrated over period 3/28-4/3/79):

At ½ mile	95 mrem		
Average 0 - 1 miles	45 mrem		
1 - 2 miles	38 mrem		
2 - 3 miles	27 mrem	166,295	
3 - 4 miles	18 mrem		
4 - 5 miles	15 mrem		2,650,000
5 - 10 miles	5.7 mrem		
10 - 20 miles	0.45 mrem		
20 - 30 miles	0.033 mrem		
30 - 40 miles	0.0023 mrem		
40 - 50 miles	0.00015 mrem		

NOTE: Using estimated risk values, these doses yield an estimate of 0.011 deaths/year.

THYROID DOSE (Integrated to infinity):

Child thyroid 5.65 mrem

NOTE: Using estimated risk values, this dose yields 0.139 cases of thyroid CA plus 0.017 deaths assuming total population is children. Calculations made using 35 picocuries of Iodine-131 per liter of milk, 2 liters/day consumption for 7 days, and a 10 gram thyroid.

has a 10 gram thyroid and assuming an unusually high uptake of 50%, I end up with a figure of 5.65 millirems to the thyroid. This is very small compared to the 30,000 millirems to the thyroid delivered by the diagnostic thyroid uptake examination. It turns out that if I assume that the whole 2.65 million people are children and all of them drank this much milk (milk dealers would like to have that be true) then this internal dose yields 0.139 cases of thyroid cancer or .017 deaths per year.

This just bears out the material that has been brought up today, that as far as we know, at least the immediate health effects have been nil and it appears to me that the future health effects are likely to be quite small.

Dr. Sternglass: Jack, I have a couple of brief questions. Number 1, I am very glad you pointed out that the bone marrow dose from a chest x-ray is only a few millirems. This brings out the misleading statements that were made by some people who compared the 80 millirem dose to the people nearby to just 2 chest x-rays. From the point of view of bone marrow dose, it was more like 25 chest x-rays. This is not insignificant.

Secondly, I'm also glad that you pointed out that the risk and benefit are shared by the same individual in the medical situation which is again not true for the environmental situation, when people who may not derive any benefit are, of course exposed.

Number 2, I wanted to mention, ask you, if you are familiar with the work of Gentry, who did find in New York State in a very careful study published in the American Public Health Journal in 1959, that individuals who were living on levels of high uranium content in New York State did have a significantly higher risk of congenital defects than people living in areas that were not living on uranium bearing rock area. Now, just one more final thing, I think one other point that I would like to get you to comment on, is the inhalation dose for the people within a few miles. This actually is perhaps much more limiting than the intake of milk. Just as you mentioned, animals breathe in the iodine and it appears in their milk, so do the mothers and I'm particularly concerned about the fact that this inhalation dose, which according to Dr. Brodsky's calculations is about 36 times the external dose per millirem, is not adequately mentioned in public media and would indeed increase the estimate of thyroid doses by, I believe, at least 30 times, 30 to 40 times. I wonder whether you could comment on that.

Dr. Krohmer: The thing about lack of exposure data was commented on some this morning. A lot of the numbers have not been released, I think I heard Niel Wald say that it was assumed that there might be a 4% increase in exposure due to inhalation. I don't know how you can claim that there was more inhalation. It would seem to me that in a reactor release, besides the gaseous products, which you won't measure later, there should also be Iodine-131, Cesium-137 and Strontium-90. You and I know the half life for Iodine-131 is 8 days, for Cesium-137 is 30 years and for Strontium-90, somewhere in the vicinity of 25 years. It would seem that, if these are also inhaled or ingested, even though we may not find the gaseous products we ought to find residues of some of these isotopes in the body. The total body counts showed nothing. Maybe you don't agree with those measurements, maybe you don't believe them. I tend to believe

them because they did measure 786 people, and probably chose them from as close to the problem area as possible and yet found nothing in their bodies.

Dr. Sternglass: Just one brief comment. Look at the paper in June 1965 of Allen Brodsky where, if you get a definite exposure from a gas cloud on the outside, you can calculate what the thyroid dose is without having to have any other information. (See Page 45 for Dr. Brodsky's response)

Dr. Oscar Powell: Dr. Krohmer, I just would like to add a commentary about the thyroid dose from the Iodine-131 uptake figure that you mentioned. I would like to point out to the audience that they should be aware that there has been concern about the radiation to the thyroid from I-131 used for this type of diagnostic procedure. As a consequence, most laboratories performing this test now have gone over to the use of I-123, which only has a half life of some 13 hours, not 8 days, and which delivers a dose of 1/20th to 1/100th of that with I-131.

Dr. Krohmer: That is true, if I-123 is pure. There is some data indicating if there is contamination in it, it looks very much like the same dose as from I-131. My friend, Fred Bruno, who is here in the audience, has some data on that, has worked on it in the field of Nuclear Medicine. He talked to me about it the other day and it turns out that I-123 is not quite as good as it looked originally.

Dr. Joseph Leaser: I practice within 1.2 miles of TMI. I have a family practice and I also teach at Hershey. I find it very comforting to see all you people from the western part of the State giving us assurances about the lack of danger. I assure you, however, that my patients do not feel this way. I also own a farm and I think that the data that you suggest about the iodine levels is really misleading. Because the farmers were much better prepared in our area than the people, they got the word out very early to take their animals inside, we got our animals inside. We fed our animals from pre-stored grain and silage; so that they were not outside, not inhaling iodine or any other particulate matter, they were not ingesting it. Also this data, I believe, was based on very low emissions of iodine at that particular time. Subsequent to that, just within the last week, we are now seeing 300,000 to 400,000 picocuries per cubic meter of iodine being released into the atmosphere, which I think is a substantially dangerous and significant level. I came to this meeting hoping to get some answers and, unfortunately, I'm leaving more concerned. I don't have answers for my patients. We are very much concerned about the effects of tremendous amounts of

radiation that have been released that haven't been told to us. For people outside the area to try to give us these kinds of assurances, I find very disturbing.

Dr. Krohmer: I would guess that your levels of 300,000 picocuries are in the plume. Do you realize that a picocurie is a trillionth of a curie and 300,000 picocuries is 300 nanocuries or .3 microcuries per cubic meter? One of the problems with using a unit like picocuries, which is used because we do not want to keep putting .00000 microcuries is that when you say 300,000, it sounds like a great big number. It really isn't a big number, if you get down to it. I am happy that your farmers knew enough to get the animals in. I didn't realize that this was true, but that may be the reason this milk data looks like it does.

Dr. Lewis Schiffer: Does anybody else have any comments on Dr. Leaser's questions?

Participant: Just a question to Dr. Krohmer, or anybody else that might be able to answer it. As I remember the fission product spectrum, we have several iodine isotopes. You have based the calculations on I-131. I-129 was mentioned earlier today from fission product data. What should we look for in terms of human exposure?

Dr. Krohmer: I know they have all been listed, but the one which is most predominant is Iodine-131.

RADIATION CANCER RISK;

WHAT IS "SAFE" EXPOSURE?*

Victor Bond, M.D.

At this time of the day, it is extremely difficult to say something that has not already been said at least once. I was to cover several subjects related to radiation cancer, considerations of acceptable risk, and the specific process by which we interpolate or extrapolate effects from effects at high doses to low doses. One aspect of this, namely somatic effects, I expected Dr. Upton to have covered in some detail. But since he was unable to be present, I do want to focus on the somatic effects and the process by which we actually make estimates at very low doses and dose rates. The things I have to say about "safe" levels of exposure are included at the end of my remarks.

Let me start with what Dr. Wald had to say this morning; with high doses of radiation, as with high enough doses of any other toxic substance, definite early effects are produced. If the radiation dose is high enough, it will kill individuals so exposed. In general, individuals who experience the early effects of large doses of toxic substances, the illness is rather brief. To all intents and purposes, the surviving individual returns to normal activities or to normal health. With carcinogens, of which radiation is one, there is a principal difference, and that is that the individual returning to normal health following the early effects of a large exposure has a probability of developing later a cancer that he might otherwise not have developed at that time. I emphasize the term "probability" here, because there is no certainty that the cancer will develop. Let me restate this as follows: Early effects of radiation, as one goes up in dose, are a certainty, and the higher the dose the more severe the symptoms. At very low doses, nothing clinical may be observed. As the dose is increased however, blood count changes occur, and at still higher dose, mild illness and then severe illness occurs in every individual exposed. With late somatic effects, however, this is not the case, and here it is an all or none situation. Almost all will live out a normal life-span. Development of a cancer is a probability, albiet a very small one, and this is versus the certainty we encounter with the early effects.

The probability of cancer induction is small even with high doses of radiation. In the Japanese, the mean dose was many rads, and yet the total increase in cancer is of the order of a couple of percent at most. In other words, most of the population so exposed go on and live out their normal life span, even at high doses. There is only a small probability of increased cancer risk, and a very small percentage of the exposed population actually develops cancer.

* Symposium on the Three Mile Island Nuclear Incident. Pittsburgh, PA., April 1979.

The principal late effect that we are concerned with at low doses and dose rates is of course induction of cancer in the exposed individual. (Genetic effects are dealt with elsewhere in this symposium.) Cancer was appreciated as an effect of radiation very soon after x-rays were discovered way back in the late 1800's. Cancers seen were of the skin, and there was good reason to believe at that time, and as a matter of fact for skin cancer even now, that this was a threshold phenomenon, i.e., there had to be a certain minimum dose before skin cancer would be induced. Accordingly, the dose was lowered, as we do with other toxic agents, and no further late effects were seen, thus re-enforcing the threshold concept. This was the condition for many decades.

The situation was changed, however, through the discovery of genetic effects by Mueller in the late 1920's when a "linear no-threshold" dose effect curve was introduced. It was very quickly assumed that something like that might happen for cancer as well. This belief was reenforced when data began to come in from Hiroshima and Nagasaki, and also from the ankylosing spodylitis series treated in Great Britain. It was found that the incidence of cancer was demonstrably above normal in individuals exposed to high doses of radiation. Thus for high doses of radiation, there is no doubt that they can cause cancer. This has been known for 70 or more years.

Now to the problem before the house, that is possible health affects following exposure to low doses of radiation. The dose effect curves in Figure 1 represent percent affected versus the dose. The problem is that, by and large, the observed data (open circles in Figure 1) are at high doses and high dose rates. The data, even at those high doses, are rather scanty in the human being. What we are interested in particularly in the context of the TMI, is what happens down in the one rad or in the millirad range.

Where there are data points, we are dealing with doses usually in excess of 100 rads of X and gamma radiation, and observed incidence of cancer is quite low even at these high doses. When we get to the lower doses, the incidence of cancer becomes much smaller, and even in very large populations direct observation of possible effects,if they exist, is inaccessible to us simply for statistical reasons.

Another reason, in addition to statistics, that we cannot make direct observations at low doses is the following: What we're looking for is cancer, and as indicated earlier today, it occurs normally and in copious quantities. We're looking for cancers caused by radiation, but in an individual who has cancer, there is no way to make an absolute determination of what was the cause of that tumor. Even if large exposure is known to have occurred, there is no absolute way to say that the cancer is due to that radiation or to some other agent. It is simply indeterminate because the types of cancer induced are identical to those that occur normally.

To contrast that with other low probability, high consequence events, consider an individual injured or killed by electrical shock, or struck by lightening. Although a victum cannot be identified before the accident, there is no questions as to cause and effect when it does happen. That is not true of cancer. We can deal only with the statistics, and we have to deal with a very small excess in a large background.

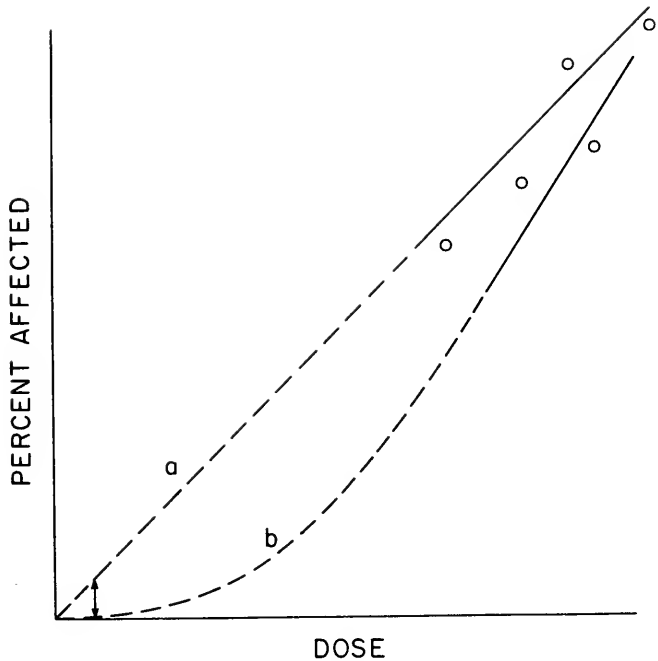


Figure 1: Schematic dose-effect curves for cancer induction by x or γ radiation. Curve a, the "linear, no threshold" hypothesis applied to the schematic data points shown on open circles. Curve b, the more radiobiologically-correct curvilinear relationship applied to the same data points. The double arrow illustrates the difference at low doses in the two modes of "extrapolation" (actually interpolation between the data points and zero excess dose and cancer incidence).

You will recall, that of all who die in the United States, about 1 out of 5 die of cancer. So there are plenty of cancer deaths, 350,000 or more per year in the United States. Looking for excess cancers due to radiation, therefore, is like looking for the proverbial drop in the bucket. That is part of the difficulty--in addition to the low incidence, one can't identify the cancer, even when one thinks it is there and is looking specifically for it.

So then we don't have direct positive observations and measurements at the low dose range of the dose-effect curve. If we want to make estimates of what happens at low doses and/or dose rates, we have to use some process of interpolation between zero excess incidence at zero dose and the observed excess incidence at higher doses and dose rates for which we have data.

What is at issue, is how should one carry out the interpolation? Curve a (Figure 1) represents the well known linear threshold hypotheses curve b (Figure 1) is a curvilinear relationship, and you see it does make a difference in the predicted incidence at low doses, as indicated by the arrows. If this curvilinear relationship is correct, then the incidence down at low doses is much lower than we would infer by using the linear no threshold relationship.

Next, I want to try to resolve to some degree this difficulty between the linear and curvilinear relationships used to predict what happens at low doses. We can't resolve it in human beings, for the reasons I have already told you about, i.e., statistical considerations will not permit direct observation. An important point I would like to make is that, if the curvilinear relationship pertains, we would expect a dose rate effect, whereas we would not expect it if the linear curve pertains. So, we might gain some information on which model applies by the presence or lack of a dose rate effect. Unfortunately in the human being, observation of this is also denied us. The data are not good enough in the human being to allow us to say definitively that there is a dose rate effect or conversely that there is not.

So we look at what happens in lower systems, where we can do the experiments and determine what the shape of a curve is. We do these experiments in a wide variety of biological systems and try to derive generalities from this that would help us in determining what happens in man.

So now in Figures 2 and 3, which are a couple of the many available examples of the types of curves that we get. Figure 2 represents chromosome abnormalities (dicentrics) induced in vitro as the radiation dose is increased. What is pointed out is the shape of the dose effect curve, and this example is indicative of what we see in a number of systems. The overall dose versus effect curve here is curvilinear. Dr. Fabrikant referred to the relationship $\alpha D + \beta D^2$, and that is quite useful for those of us who like models. This model was first applied to these data, way back when, by Lea and by Karl Sachs. An $\alpha D + \beta D^2$ relationship does fit precisely at low doses as you see in the blown up inset for the low dose range. These data are fitted overall by a quadratic function with a definite linear component. But here again, you see very sparse data; one point at 10 rads, one point at 5 rads, and even these few points are obtained at a tremendous expense of technicians' time.

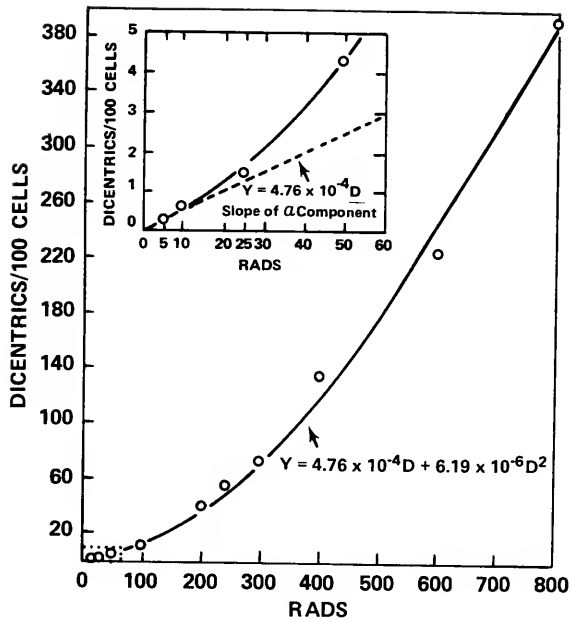


Figure 2: Frequencies of dicentrics in human lymphocytes exposed to x-radiation doses ranging from 5-800 rads (250 kVp x-rays, 100 R min^{-1}). Over 14,000 metaphases were scored to obtain data for the 5, 10, 25 and 50 rad points. Insert is an expanded graph showing data at low dose points, and the slope of the α coefficient. (Redrawn from data D. C. Lloyd et al., 1975)

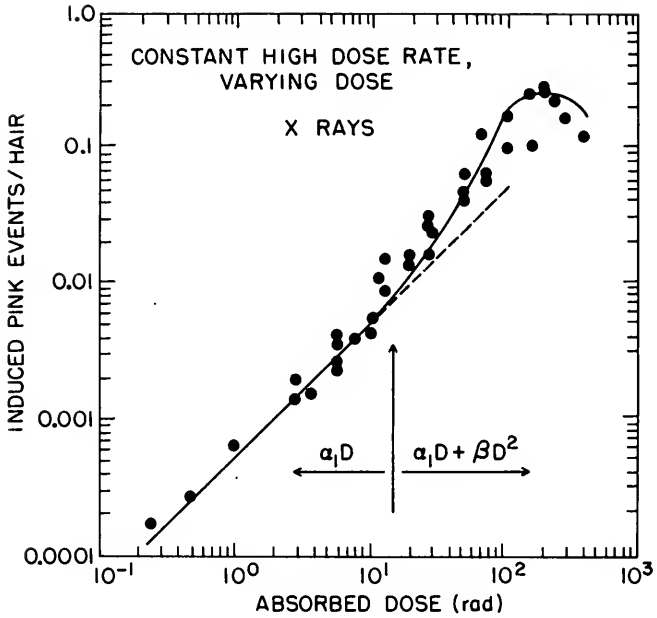


Figure 3: X-ray dose-response curve, induced pink mutations in Tradescantia, on log-log plot to show detail in the low dose range. The solid circles indicate experimental points at high dose rate. Note that the low dose portion of the solid curve and its dashed-line extrapolation have a slope of unity, corresponding to a linear, no threshold dose-effect relationship. The increased slope at higher doses indicates that the response in the higher dose range involves a higher exponent of dose. See text for explanation of the "$\alpha_1 D$" and "$\alpha_1 D + \beta D^2$" portions of the curve (data of Sparrow et al, 1975; Underbrink et al, 1976).

Now, in Figure 3, let me show you another system where we can get even better data, and now we go down to a quarter of a rad (250 millirads) or so. This system was referred to this morning. It is Tradescantia; spider wort is the common name. This is on a log - log plot. The point I wish to make here is that this is the same curvilinear relationship you saw in Figure 2. Here, however, you can see definitely the linear component down to the millirad range, and also the dose squared component at intermediate doses. I won't deal with the part that goes "over the hump" at high doses.

To illustrate the amount of effort in doing the experiments to measure these data, to get one point down here, for instance, about 250 millirems, one has to count about 10 million cells. The spider wort is designed by nature very nicely, so that one can actually make the observations relatively easily (but still only with painstaking lengthy effort). It takes 2 technicians about 2 weeks to obtain that one data point--10 million observations to get that. The point that is evident here is, if one can and will make the effort to get the data in these simple systems, then one can determine the shape of the curve to very low doses. In mammals or human beings, however, the size of experiment necessary to get such data is simply prohibitive. (Imagine 10 million "exposed" and a like number of "unexposed" people, to obtain only one point on a curve!)

Thus in simple systems, in essentially all systems having complete cells (eukaryotes), the observed relationship is so called linear-quadratic.

Now we go to animal systems and study the end point of interest, i.e., carcinogenesis in animals, mainly in mice. The same curvilinear relation is seen in Figure 4 where ovarian tumor incidence vs. absorbed dose are plotted. I'll show you only one tumor system; I could show you many more. The solid circles represent the dose effect curve for high doses and dose rate. A curvilinear relationship with perhaps a threshold is seen. Now let's consider the curve for low dose rate (open circles). It is clear that at a dose of 50 rads the effect is much less at lower dose rates, i.e., a marked dose rate effect exists.

To sum it up briefly, experimental data in a wide variety of systems suggest that the overall relationships at high doses and dose rates is curvilinear. If we reduce the dose rate, we get the substantial linear component, indicating a strong dose rate effect. In no system, with one apparent but questionable exception (I won't go into it unless someone is particularly interested), do we find the so called linear no threshold relationship. Throughout the animal and plant kingdoms, and for essentially all end points looked at including carcinogenesis, the relationship holds. So one would conclude that the human being would be strange indeed if he were unique as a species and unique for that specific end point, carcinogenesis. Thus it is most unlikely that the relationship for man is, in fact, linear rather than curvilinear as we see in all of the other systems.

Now, let's deal briefly with the human data. In order to do the necessary interpolations to include low doses and dose rates, it is mandatory that we have several dose points so that we can perform some kind of analysis to determine what the curve shape might be. The principal examples of data we have, that we can work with, are from Hiroshima, Nagasaki, and from the

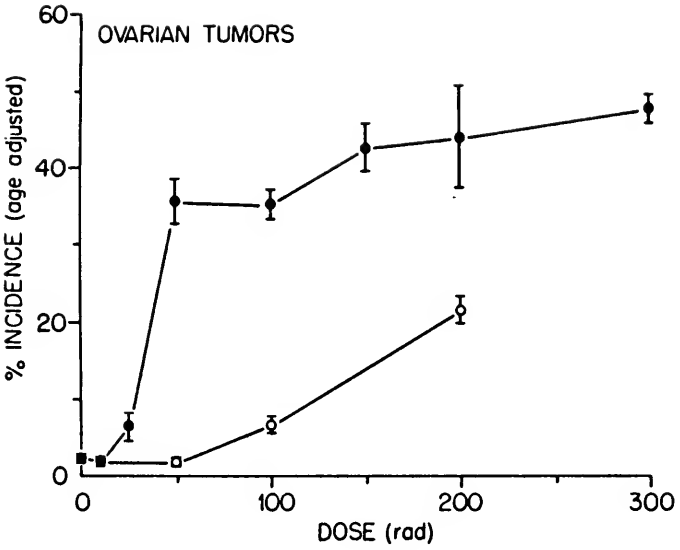


Figure 4: Incidence of ovarian tumors in RFM mice after ^{137}Cs gamma ray irradiation. 45 rad min^{-1} solid circle; 8.3 rad d^{-1} small open circle (Ullrish and Storer, 1978a).

ankylosing spondylitis patients. Figure 5 shows the Hiroshima and Nagasaki data. We will not talk further about Hiroshima because a large component of that dose is fast neutrons with a different shape expected. We're interested here principally in X and gamma radiation, and hence we shall deal only with the curve for effects in Nagasaki, where the radiation was essentially pure gamma (similar to x-rays). Now the total number of patients in this series with induced leukemia is low and the total number of individuals exposed is relatively high, (I'll speak more about that in a moment). The total number in Nagasaki with leukemia, only leukemia, was about 16 cases. So the statistics are poor. But just on the surface, this curve does seem to be consistent with a curvilinear dose-effect relationship, although one could not say definitively that it is in fact curvilinear because one could also accommodate a linear relationship here. The main point I wish to make, however, is that it's often stated, and you've heard it stated many a times today, that we don't know what happens at low dosage. Now, that in a sense, is true, but in another sense, it certainly is not true. We have a large amount of data, but none of it demonstrates an effect--the results are "negative" in the sense of indicating zero effect.

Let me be specific. A large number of exposed persons are represented here in Figure 5; the doses range extends from a high of well above 100 rads, down to zero. Let's focus on the low dose range for just a moment. You will see that where the points are, the risk of leukemia is actually less than the unexposed control population. I don't make anything out of that at all, beyond that it shows no effect, or is just not different from the controls. But the main point I wish to make is that in the dose range from 1 to 9 rads (1,000 to 9,000 millirads), there were 20,000 individuals and the mean dose there was about 3.5 or so rads. That represents 20,000 times 3.5, or something like 70,000 person-rem of population exposure. That is a large number of individuals exposed in a so called low dose range and there is a total absence of demonstrable effect even after 25 or 30 years. Now that doesn't mean there cannot be some minute degree of effect, but it does mean to me that, based on observations on that large number of person-rems of exposure, the chances are extremely small that leukemia incidence could be any worse than that represented by the linear no threshold relationship. In other words, the risk has to be less than linear model predicts. So, it's just misleading to say we do not have any information. We have a great deal of information and the information is negative, i.e., no effect at those low doses, even though the total person-rem of exposure was very large (contrast this 20,000 person-rem of exposure with completely negative results with the total of perhaps 2,000 or 3,500 total person-rem for the current TMI incident, to appreciate the absurdity of spending public money to mount a so-called epidemiology study to study possible radiation effects on the TMI "exposed" population.

In Figure 6, you see again, schematically, the curvilinear relationship discussed (curve A). This is what we see in most animal systems. Now, the linear no threshold relationship that you hear so much about is this dotted line B. It's simply a line drawn by interpolation between the observed data at high doses and the origin, (zero excess dose and incidence of effect). The "risk coefficients", which I'll talk about in a moment, are represented by the slopes of the lines, or the effect per unit dose. Using the linear no threshold hypothesis means that we assume that the same slope seen at high doses

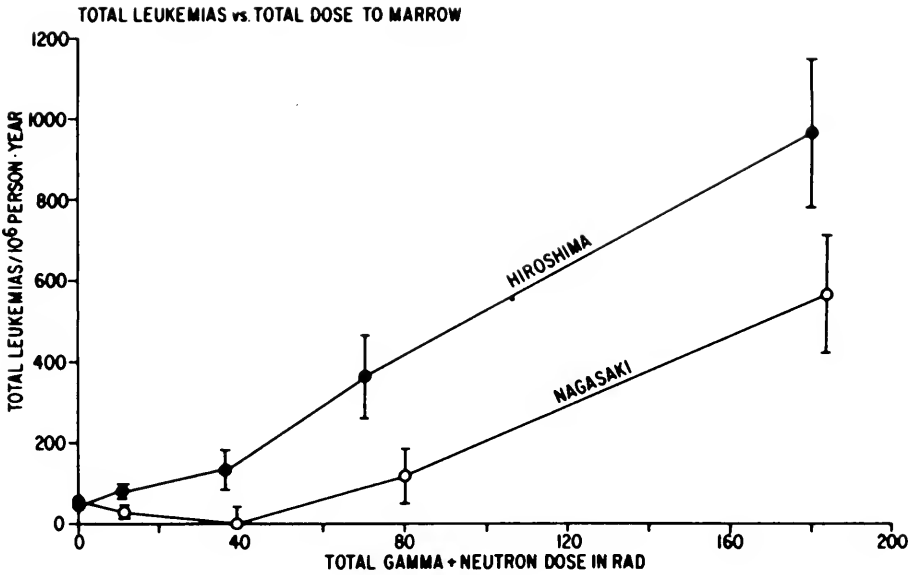


Figure 5: Total leukemias vs. total dose to marrow. Standard deviations in incidence rate are shown. The effectiveness of the radiation was greater at Hiroshima (neutrons plus γ-rays) than at Nagasaki (almost entirely γ-rays).

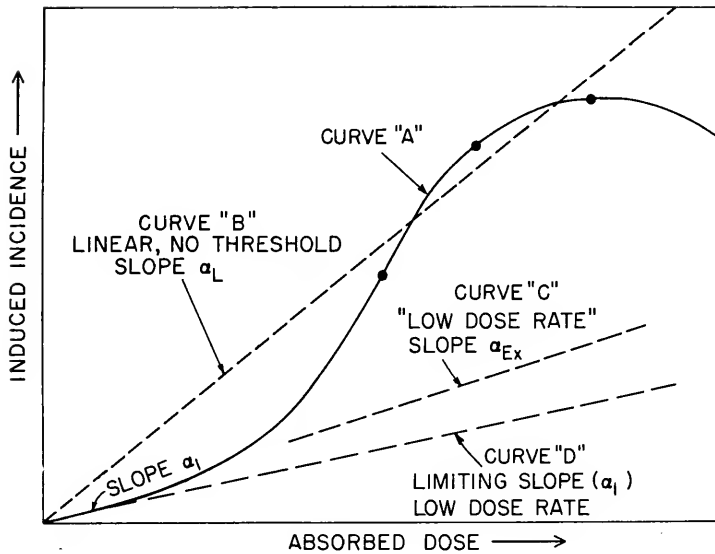


Figure 6: Schematic curves if incidence vs. absorbed dose. The curved solid line for high absorbed doses and high dose rates (curve A) is the "true" curve. The linear, no threshold dashed line (curve B) was fitted to the 3 indicated experimental points and the origin. Slope α_1 indicates the essentially-linear portion of curve A at low doses. The dashed curve C, marked "low-dose rate", slope α_{Ex}, represents experimental high-dose data obtained at low dose rates. This experimental low dose rate curve may, in principle, at very low dose rates, approach or become indistinguishable from the extension of the solid curve of slope α_1, the dashed curve D labeled "limiting slope (α_1), low-dose rate".

where data exist, holds all the way down to the extremely low doses, and even to where the line enters the origin. Now, all of the biological data tells us that reality isn't like this--the curve is not linear--and that the more correct relationship is curvilinear represented by the solid curve A in Figure 6. As one comes down in dose, one comes to a straight portion of the curve, (slope α). It is also linear to be sure, but the slope is substantially different from (less than) the slope of the so called linear no threshold line. Figure 6 also shows the effect of dose rate. It shows that if we take a high dose of radiation, keep this high dose the same, (constant) and simply lower the dose rate, the effect will come down to lie on a curve such as C. Ultimately at very low dose rates, the curve will reach the slope of curve D (slope α_1) as that of the low-dose end of the solid curvilinear line A. So that, by this model, coming down in dose on this solid curve A gives you the same ultimate result as using high doses and coming down in dose rate. What this means in overall summary, is that according to this model and from the animal data, using the linear no threshold hypothesis over-estimates the actual risk by a factor that depends on the precise tumor system. There are various values attached to this over-estimate and it's of the order of or in the range between 2 and 10, with perhaps 5 as an average value among tumors.

What I am telling you here is derived from radiobiology, and represents what a sizable group of radiobiologists believes is the most probable situation, i.e., that the linear quadratic (or even a pure quadratic) is the true dose response curve even for tumorigenesis, including in the human being. This curvilinear relationship (curve A) is a more correct model than is the "linearity" model. For some systems, this initial slope (α_1) might be lower than that shown, and for some tumors it might actually be zero, i.e., there may actually be a threshold.

In the 1972 report of the "BEIR I" committee, frequently used to make risk estimates for radiation exposure situations, a dose rate effect was not taken into account. It's the linear no threshold hypothesis (dotted line, Figure 6) that is used to be conservative, and most individuals would consider that that approach overestimates what the true risk is. So in order to be conservative, to err on the side of safety, that is the process that is used for risk estimates for public health decisions. Again, we don't have data down at very low doses, not because we don't look. The population of the U.S. has been looked at in the context of background radiation and actually no excess cancer was found. If anything, it's the reverse; where the background radiation is the highest, the cancer rate observed is the lowest. So look as one may, one cannot find any effect at very low doses, and the approaches to estimating these nonobservable effects (the "linear hypothesis") is conservative.

In all of these committees, there is an evaluative process. One looks at the human data and there are many sets of human data. The "BEIR I" committee report represents a near-Manhattan- telephone-book size document full of data used in the evaluative process. Some pieces of information,some selected pieces of information, would indicate that maybe this initial slope is in fact the same as linear no threshold, and some rare pieces might even suggest that the risks for some tumors is higher than that. On the other hand, there is an equally large (and equally questionable) set of data that suggests that there may be a threshold and the risk at very low doses is zero. Thus a Committee,

if it wished to highlight questionable data, could "show" either that radiation is considerably more hazardous than usually stated, or completely without hazard at low doses.

What a committee actually does, is to look at all of the risk estimates and look carefully at the methodology and put most reliance on the most reliable data. There is general agreement among the committees; BEIR I, probably BEIR III, the UNSCEAR and other international committees of experts that have gotten together and looked at this kind of data. Their risk estimates do not differ markedly. The consensus is that the linear no threshold model probably represents an upper limit. I have not seen the BEIR III report, have not had access to it, but from what I hear from Dr. Fabrikant today, if anything, the (upper limit) risks that the group is coming out with in BEIR III are less for cancer than those we developed earlier in BEIR I.

Now then finally, let me bring what I have said directly home to the TMI situation. From BEIR I, the overall number that has been widely used by agencies and groups such as the EPA, NRC, ICRP, UNSCEAR, etc., for the overall cancer risk, the single (upper limit) number is 200 excess cancers of all types over all time following exposure of each of 1 million people to 1 rad. Let me restate that, it's 200 excess cancers per million people per rad, and that is the yield over all time following the exposure. That is sometimes expressed as per year also, which involves dividing 200 by the total number of years during which one expects the near-total yield of tumors. So then the number to use in connection with the TMI incident is that the upper limit of 200 per 10^6 person-rem over all time, or about 10 per million person-rads per year, for 20 years. And then, if we have the exposure in person-rem, it's very simple to calculate the upper-limit excess risk--it is simple proportionality. The number I heard before was 2000 for the total person-rems from the TMI exposure, and I heard today that this may increase to about 3500 person-rems now. If one goes through that simple proportionality calculation, it yields an upper limit of less than 1 additional cancer death over all time following the exposure at TMI. Introducing the "dose rate" factor, the expected yield would be a very small fraction of one cancer.

In order to put the TMI radiation exposure further in perspective, let us now consider what might be considered to be "safe" exposure. Since "safe" and "unsafe" are highly relative terms with definitive meaning confined to the mind of the beholder, only comparative information can be provided to aid each individual in formulating a personal view. Low-level radiation exposure to man made sources properly belongs with that large class of human activities involving the use of potentially hazardous chemical or physical agents, the use of which is generally considered to be "safe" if conducted properly (includes many drugs, home and garden chemicals, exposure to sunlight, use of electricity in the home, swimming, auto and air travel, etc., etc.). For any one of these agents or activities the admonition can be applied, that there is no sharp boundary defining a safe or dangerous level of exposure, and that "any amount of exposure (use, or 'dose') carries a probability, however small, of serious harm". The inverse of this statement also holds equally well, that "the probability is very high that any small but proper use of (exposure to) these agents will be completely without serious harm, now or in the future." The overall effort must be aimed at reducing the small residual risk of harm to the

minimum that will permit continued availability of the benefits. Continued use or abandonment of the agent must then ultimately be adjudicated in the public market place, usually through the political process including regulatory agencies.

It might be argued that low-level radiation should be placed in the "Delaney Amendment" category, which adopts the approach of zero allowable risk for chemical carcinogens. Although background exposure cannot be avoided, the option of zero additional exposure can in principle be elected. This would of course totally preclude such individual benefits as diagnostic X-ray and nuclear medicine, and such collective benefits as nuclear power and the myriad other benefits from the uses of radiation in industry. The first is an individual, and the second a societal decision, and there is no soft path to having the benefits of either without the risk.

It is understood that the individual doses received at the TMI Power Plant are all less than 100 mrem, yielding an average dose of one millirem or less. The collective dose is about 2000 person rem (could be as high as 3500) to the two million people within 50 miles, yielding a health impact (BEIR, UNSCEAR) of less than one additional cancer death over the next 30 or more years. The "safety" or "danger" of this exposure can be assessed (to allow evaluation; not to justify) against the approximately 100 mrem average yearly exposure to everyone from natural background radiation and an equal amount from diagnostic exposure. The added 1 mrem is to be compared with the approximately 7,000 millirem the "average" individual of about 35 years of age will have received from these sources. The 2,000 person rem exposure may be compared with the value of about 400,000 person rem received annually by the same population from natural and medical exposures. To compare the less-than-one cancer death over 30 or more years, the relevant background is a total of about 600,000 deaths in the same population area over the same 30 years, of which 120,000 will be from cancer. The probability of any one of the exposed individuals dying of cancer is increased from the normal of about 19 per cent, by less than 0.002 per cent. It is comparative figures such as these that should aid one in judging the "safety" or "danger" of the radiation exposures sustained near Harrisburg.

1) The Effects of Populations of Exposure to Low Levels of Ionizing Radiation, (BEIR Report). National Academy of Sciences, National Research Council, Washington, D.C., November 1972. (1979 revision about to be issued.)

2) Sources and Effects of Ionizing Radiation, UNSCEAR Report, United Nations, New York, 1977.

3) Basic Radiation Protection Criteria, NCRP Report, No. 39, Recommendations of the National Council on Radiation Protection and Measurements, Issued January 15, 1977.

4) Review of the Current State of Radiation Protection Philosophy, NCRP Report no. 43, Recommendations of the National Council of Radiation Protection and Measurements, Issued January 15, 1975.

5) Annals of the ICRP, ICRP Publication 26, Recommendations of the International Commission on Radiological Protection, adopted January 17, 1977, Pergamon Press.

6) Why be Quantitative about Radiation Risk Estimates? by Sir Edward E. Pochin, Lecture No. 2, in the Lauriston S. Taylor Lecture Series in Radiation Protection and Measurements, National Council on Radiation Protection and Measurements, presented March 15, 1979, issued July 1, 1978.

Dr. Sternglass: I'm glad to hear that you did say that we might have at very low doses a slightly higher risk than might be extrapolated by linear hypothesis because I imagine you are referring to such work as by J. W. Baum at your laboratory who considered the possibility of a fractional dose response that might give a slight upward curvature near the origin. I imagine there is some indication of that in the Mancuso-Stewart analysis of the Hanford workers. I think, therefore, you are right; we don't know all there is to be known about the extremely low dose and low dose rates.

Dr. Bond: I am aware of what Dr. Sternglass is referring to. In Dr. Baum's analyses, he used mainly high LET radiation instead of the low LET radiation in which we are principally interested here. In reviewing a number of radiobiological systems, we have not found any instances of dose-response curves such as those referred to by Dr. Sternglass, for low LET radiation. I do know the Mancuso-Stewart data, and as I am sure that Dr. Sternglass is aware of, there have been a number of rather extensive papers critical of those studies. The articles conclude that any implication that radiation alone caused the effect reported simply is not justified by the experimental data.

Dr. Shrivastava: Well, I'm sorry we have lost some of our audience because they did come on planes and they did have reservations. We have also lost at least one of our speakers, he had a plane to take to go back to California. We will have a panel discussion, for a short time. Because of the shortage of time I would like to set down some ground rules for the questions to be asked of the panel. I would first like all the speakers to take their seats on the panel, if they will. In order to be fair to those of us who are probably shy of getting up on the microphone we have decided that we will ask them to write down their questions to the panel. So will you please, any questions from anyone is welcome. Please write down your questions, a sheet of paper has been provided to you in the folder for that purpose. We will avoid the use of the microphones except by the speakers.

Dr. Brent: Dr. Shrivastava, while we're waiting, maybe some of the members of the panel have some comments, I know I do.

I was sitting in the back of the room during the proceedings and I understand many of the people who have come here are physicians in the state, interested in knowing more about the radiation, in order to answer questions from their patients. Some times when we make a theoretical presentation with regard to animal experiments and human populations, it's hard to translate that into information on a question to question basis when the patient asks you a question. I think that some of the questions that your patients may ask you, you should be able to provide answers. When you can't provide an answer you have to say so but even more important, remember that when you are taking care of a patient, I know that when I take care of a patient, I don't relate only to the one question that is being asked. I think it's a moment of good preventive medicine in when a patient brings up a discussion like this. Let me give you just a couple of examples.

It's very clear to me that if a woman comes in and was either pregnant, is pregnant or got pregnant after the Three Mile Island accident and says to you, "Dr. do you think I should interrupt this pregnancy?" I think it's very clear on the basis of the exposure here at Three Mile Island that you should support her to continue her pregnancy, unless she had other reasons for it's interruption. It would be irresponsible on your part to create a feeling in her that she should interrupt this pregnancy from this radiation exposure. Similarly if she says, "Do you think that my baby is going to be malformed from what happened at Three Mile Island?". I don't think the data will indicate that this is a possibility at these low levels although you again as a physician have the opportunity to point out to her that once she's

pregnant she has a good chance of having something go wrong and you as a physician are not in the position to guarantee the outcome of her pregnancy. Also, when you get down to the leukemia data Dr. Bond referred to, if your patient is sitting there and smoking then this may be your one opportunity to point out to him that there are 96 thousand deaths a year, most of carcinoma of the lung, mostly related to smoking and if you haven't been able to convince him to stop smoking till that time you might point out to him that his risks are thousands of times greater that he's going to incur a carcinogenisis risk from the fact that he's smoking than he is from being in the Three Mile area. So I think you can utilize some of this information presented today into a Doctor-Patient relationship on a one to one basis that may be meaningful and helpful.

Finally, Dr. Sternglass referred to Gentry's article. As you know I did have that on the slide. He talked about the higher incidence of congential malformation in high background radiation. Gentry's article, that's a terrible article. That was one of the basis that is was redone by the group at University of Chicago and the epidemiologist at the CDC to point out that it had major flaws, even a lack of understanding of the etiology of malformations and disregard for most of the basic tenets of epidemiology. You can't use bad experiments to prove a partisan viewpoint. You know that you've got to take all the data and when it's confusing you got to admit that it is confusing and I just don't see how you can use an article like that to prove anything.

Question: What are the facts that we have on the specific concentration of radioactive fallout in plant or animal life. How do these facts relate to food sources that are dangerous in areas of plume coverage?

Dr. Brent: Well, I'll just make a few comments on that. The radiation physicists can comment on that more appropriately. You know fallout is a radioactive material which deteriorates and therefore depending on the length of a half life of the material as days and weeks go by the material disappears. Therefore, the danger would depend on dosage and the time that you evaluate it. It just so happens in this particular incidence, even from a theoretical standpoint it was a fortunate season because of the fact that there were no food products growing at the time in the fields and the animals did not have availability to food that had been contaminated from fallout. So that the only isotopes at these low levels that could be incorporated would be by inhalations. I don't know whether I've answered the question, did everyone else hear the question and does anyone want to comment on it?

EDITOR'S NOTE: The Department of Energy (DOE) analysed a large number of

samples of environmental soil, grass, surface water and air samples in the path of the plume. The measurements included gamma spectrum analysis to detect, identify and quantify amounts of radionuclides present. The analysis showed that 97 percent of the samples had no radioactivity. Only 3 percent of samples showed I-131 barely over the detection limit and well within the permissible concentrations. They concluded that the predominent radionuclide in the airborn discharge was the inert gas Xe-133 (half life 5.3 days) with a small amount of iodine-131 (half life 8.0 days).

Question: Could a brief characterization of the difference between Alpha, Beta and Gamma radiation and their biological effects be given?

Dr. Krohmer: The answer is yes, but I'm not sure in less than a week or so. I meant to say something during my presentation because Dr. Brent for instance had 'R' up on the slide and he'd say 'rem' or 'rad' and so forth, they seemed to be interchangable. That is true for gamma radiation and beta radiation only because the relative biological effectiveness which relates 'rads' and 'rems' tends to be essentially 1.0 for these radiations. So you can use things interchangably. Alpha radiation is a particulate radiation, a very bulky massive particle which loses energy rapidly because it's not moving very fast. It tends to have high concentration of energy deposition along it's path. This high linear energy transfer (LET) in mammillian systems tends to be more effective biologicaly because in mammillian systems it helps to have a lot of energy transferredin a locus. So the biological effects of a given amount of alpha radiation, a given dose in rads, will be more than the biological effectiveness of the same dose of Beta or Gamma radiation. I think that's probably as far as I should go on this.

EDITOR'S NOTE: Alpha particle is the charged helium nucleus, beta particle the negatively charged electron and gamma radiation are uncharged photons or simply electromagnetic waves. The energy transferred by high frequency beams of these particles, per unit path length is referred to as Linear Energy Transfer or LET. The LET depends on the type of particle i.e. its mass and charge and its kinetic energy. Alpha particles have much higher LET compared to beta and gamma rays. The Relative biological effectivenss (biological effect per rad of energy absorbed) increased with increasing LET. In health physics the average effectiveness, also called 'Quality factor' is considered to be 10 for alpha particles and 1 for all gamma radiation and 1 for beta radiation if Emax> 30 kev. For beta beams with Emax< 30 kev, the quality factor is taken to be 1.7.

The quantity called 'dose equivalent' is defined by dose

absorbed times Quality Factor and is expressed in units of rems.

If QF = 1, rads and rems are equivalent, but for alpha particles, 1 rad dose is equivelent to 10 rems.

Question: How do most of these studies, based primarily on low LET, get extrapolated to high LET?

Dr. Bond: I don't think that there is a process of extrapolation involved. Incidentally, LET refers to Linear Energy Transfer and the low LET radiation are x, gamma and electrons. High LET radiations are alpha, fast neutrons or really the recoil protons from fast neutrons. The density of the ionization is greater for the high LET than the low LET. We actually have data in a number of biological systems for the high LET radiation directly, so it's not necessary to perform the extrapolation. For the human being, we do have direct information from Hiroshima external beam of fast neutrons. We do have risk coefficients there and the slopes of the curves. For internal radiation, we have very extensive data from ingested radium, radium gives off alpha rays and that is high LET radiation. The high LET radiation is not relevant to the Three Mile Island situation, since the only exposure to the public or actually, of individuals in the plant in connection with that accident came from low LET radiation, there was no high LET involved.

Question: This is a question concerning the exposure estimates. How can you be so sure of your exposure estimates when most dosimeters were not installed until Saturday night?

Dr. Wald: What I have given you is preliminary and tentative estimates which are under revision currently. Sureness is a relative term. The reason for accepting them at this time is that there is independent check by other systems than the TLD. Particularly, the actual measurements of the plume began within 12 hours after the exposure. The correlation between the meteorelogical data on which the plume was translated into area exposures was very good when actual samplings were made. Most of the measurements checked with the data calculated from the model. And this was repeatedly done throughout the episode. A group at Livermore Laboratory had already generated the models and could predict, based on the meteorology hour by hour, exactly where and how much activity would be at what distance and the correlation of actual measurements and those predictions were excellent, so there is an independent check on the TLD system. It's true there were only a relatively small number of dosimeters in the field early on, for the reason that was already noted. The impression that I get from speaking with the various groups is that further refinements may give a factor of perhaps 2

increase in the numbers that we used for person-rem or for the worst case individual. There are other things going on independently for futher confirmation of the cumulative exposures and the validity of observations, I've given you such as the corraling of photographic film at the various points where suppliers maintained film throughout the region. Densitometric checks will be made. This is the study that FDA is doing with Eastman Kodak and it's just getting underway. So that there will be a number of other approaches and that gets down to accumulative exposures, depending on the film and the conditions of storage perhaps, quite readily 50 MR and below as anyone who's gone through too many screening devices at airports can attest.

Question: Will the written proceedings of this seminar be available in published form?

Dr. Shrivastava: Our intention at this time is to make such proceedings available. I think we will need about three months to be able to come out with the published proceedings. Any of you who would like one are requested to write us a letter and we will respond to you in about three months time when it will be available.

Dr. Brent: I was interested in the comment by the physician who said he came here, and he spent the whole day here and he is more confused. That's hard for me to understand. I would like him to explain what he (see comment by Dr. Leaser page 121) is more confused about. Also the inference that because a person was not in the area therefore he doesn't have the capacity to evaluate the problem, I don't understand that. That doesn't make sense to me and I would just like to know what is the basis for these statements, except that I noticed that three news reporters went to talk to him afterwards.

Dr. Abrahamson: Probably my genetics!

Dr. Brent: I think there is a lack of communication about these risks. I tried to put this in the words that you could talk to the patient about this. The physician has a potential for being a very good educator. We also talk about the physician as being an ombudsman, a protector of the patient. You are on his side, therefore you want to tell him the truth and he's going to believe you. What could you possibly say that couldn't be helpful. There's nothing like knowledge and data and the facts to take away anxiety and make a person more able to handle the situation. So that if you came and you learnt anything today that you didn't know before, it's got to help you out in dealing with the patients.

You see I get two to three calls a week from panicky women who have been told by physicians after getting a chest x-ray before they were pregnant that they are going to have a malformed baby. So that the ignorance among our own profession with regards to radiation hazards and anxiety in that area is very bad. You know this is an area where we have to have responsibility. If you are going to convey something to a patient, you better tell him the facts and not add to the disease.

Question: Is genetic malformation such as Downe Syndrome greater in first or second generation children of parents exposed to radiation?

Dr. Abrahamson: I guess the best estimate I can give you is that the first generation effects should be larger than the second. As I described and showed you a chromosome picture of those individuals that carried translocations you could get Downe Syndrome in a second generation if the parent were a carrier of a type of translocation. The frequency of that event would be lower than the initial frequency of Downe Syndrome induced directly.

Question: Is there really a distinction made between low LET X, and gamma radiation?

Dr. Abrahamson: Based on a committee that I've been serving on under the direction of Dr. Bond for the National Committee on Radiation Protection, all of the carefully developed data that I have seen and Dr. Bond showed you some of these very elegant chromasome pictures in genetic analysis, the answer seems to be that low LET x-rays given at low dose rates is more effective than low LET gamma given at low dose rate by approximately a factor of two.

Question: What kind of gamma and what kind of X?

Dr. Abrahamson: How do I define X as opposed to Gamma? X is delivered by an x-ray machine and gamma is delivered by a cesium source or a cobalt source.

Dr. Bond: Yes it's defined by energy. The low energy x-rays are more effective per rad than are high energy x-rays or gamma. You must clearly differentiate between very high doses and dose rates where the difference is in the order of 10 to 25% and you are dealing primarily with the D^2 part of the overall effect. If you get down to low doses, low dose rate, you get rid of the D^2 you are now dealing only with $\alpha.D$. The difference in the $\alpha.D$ slopes is approximately 2 or 3 depending on the energy. So it's a very real thing seen in a number of different biological systems. This is the effect per rad or per unit dose. The high energy gamma rays are

less effective than are the low energy X.

These are observations, these are not theory.

Question: What is the mechanism? I don't understand the reason.

Dr. Bond: I leave it to you if you are a radiation physicist to tell me what the mechanism is. I'm telling you that the data show a factor of two difference in carefully investigated experiments. If you want to give us your name, we'll send you the data.

Question: Is it true that the new BEIR report will show lower risk estimates than the BEIR '72 report?

Dr. Abrahamson: I think the answer to that is yes, although I'm not sure about the somatics report because I haven't seen the final version of it. But certainly, for the genetic report, there are a factor of two differences between BEIR '72 and BEIR '79. I tried to allude to the reason for that. BEIR '72 used doubling doses in the range of 20 to 200 rems. BEIR '79 used doubling dose in the ranges of 50 to 250 rems. So you have roughly a factor of two for the highest relative mutation risk. And that's the main difference in the genetics report. If I'm reasonably correct on the somatics aspect of the BEIR report, I though Fabrikant said that there are 70 cases of cancer over lifetime per rad exposure per million, whereas if I'm quoting Bond correctly that there are about 200 cases for the same over-all exposures. Therefore, you roughly have a factor of three differences in risk estimates if one was BEIR '79 and the other was BEIR '72. But we would like to see the actual manuscript before the question can be firmly answered.

Dr. Krohmer: Judging from the numbers Fabrikant gave on cancer production, it sounded like a reduction to me, because I had a number from BEIR '72 of seven cancer deaths per rad per year per million people and he said 1 to 5 so that's a fair reduction.

Dr. Abrahamson: I wanted to make one other comment. One of the reasons I didn't spend a lot of time on the UNSCEAR report with respect to genetic effects is that the UNSCEAR report used only male data, it did not attempt to risk estimate for female data. So therefore their doubling dose of 100 rem which is a single doubling dose point is based on speratogonial radiation exclusively. BEIR committee used an average for both sexes including female data. So there is a difference. Since the UNSCEAR report says to ignore the female contribution to mutation, I thought that's a very dangerous thing to do, in addition to the ERA consideration.

Question: The HEW task force, that's the Libbasi report task force, and the Bureau of Radiological Health have both asserted the need to reduce x-rays medical exposure by as much as 25 to 30%. Is it true that most of these x-rays are being done in the interest of 'defensive medicine'? To put it bluntly, many people including professionals, think that these x-rays benefit the doctors and not the patients. Please address this issue including dental x-rays. I understand there's a wide difference in exposure depending on the type of equipment used by dentists.

Dr. Krohmer: Well that's a loaded question. I think all of us, everybody in the medical field, would like to decrease exposures even further. We have already decreased medical exposures for individual exams. Now maybe volume goes up and the overall integrated or average population exposure doesn't change. It is true, that there's a lot of x-ray examinations that are carried out for defensive purposes, medical-legal things have been just horrible in the last few years. I must admit that many physicians are running scared because there are so darn many malpractice suits and so many malpractice judgments that they hate to, in case of accident and things like that, leave anything undone that might help a little bit. In many cases I think they get their malpractice suits that get awarded because they didn't do something. There is no question that there is a problem there. I think we have to straighten out this whole malpractice situation. I think this this could cut down exposures. Another thing that could cut down exposures is the use of x-ray by trained people. The last figures that I saw were about 5 or 4 years ago and more than 50% of x-ray examinations were carried out by non radiologists, private offices and so-forth and this sort of thing probably is not good. Everyone, I think agrees that the people who at lease perform the x-ray examinations should be as well trained as possible. I would think that could help a great deal. Maybe that would take care of the 25 to 30% reduction. If we do both of them it would be down even further. In regard to the dental x-rays, it is true that there is a wide difference or a significant difference in the amount of the exposure to the patient, based on the type of equipment used by dentists but also by people who make radiographs of other portions of the body. These wide differences are getting to be less and less because we have state regulations and federal recommendations on various parameters that are used. I think the differences now are much less than they were 5 or 10 years ago. But, there are differences depending on the length of cone the dentist uses, the energy, the setting of the accelerating voltage, type of filtration, etc. Filtration is pretty much taken care of now-a-days. There are regulations in practically every state. I think that's probably as far as I should go on this, it's a very good question.

Question: What if any, measures of public education, seminars or TV programs are planned to help clear up some of this public anxiety and provide local citizens any opportunity to discuss with health professionals the consequences of low level radiation and benefits of some types of radiation?

Dr. Wald: Well hopefully this program for which I think we're indebted to the National Cancer Institute and Allegheny General Hospital is a step in that direction. This is a question which I will be glad to pass on to Dr. MacLeod who is the head of Public Health for the Commonwealth of Pennsylvania.

Dr. Abrahamson: I'm a member of the Wisconsin State Board of Health, Radiation Protection Commission and I'm trying to get through the state presently a sort of accreditation ruling for radiation technicians and we don't have one in our state. We don't have licensing for technician or an accreditation. Do you in Pennsylvnaia have a ruling?

Dr. Krohmer: This is in the works right now for licensing which requires training and an examination for everyone. I don't know how far that has gone, do you Niel?

Dr. Wald: It died in the last session but it has been proposed again as a modification of the whole radiation control act.

Dr. Krohmer: I would guess that Three Mile Island is going to help to grease the skin on that. Most of us feel that it is a good idea, I think people have felt that the medical field was against it. I guess there were people against it and for various reasons. I was in New York state when licensing went in. The way it was handled originally was very poor. There were people who were grandfathered in, who were just the type of people that the licensing was trying to keep out. There were some initial examinations that were given to people with a lot of experience but not much training that were farces. We're going to have to wait for normal attrition for those people who were let in on a grandfather basis to eventually get out of the field. In Pennsylvania, I was on the initial committee and I fought strongly, and I think everyone did, that everyone that came in and got a license had to take an examination. Now if they were registered with the American Registry of Radiologic Technology they had taken an examination and in all probability this would be accepted. If they hadn't they would have to take a meaningful examination. I hope that stays in it when and if it finally gets through.

Dr. Shrivastava: Well that ends our questions. I'm very thankful to all of you who have taken your time to come to this meeting. I hope it has been useful.

National Cancer Institute

January
1980

NIH
Publication
No. 80-2087